NATURE

A Weekly Journal of Science

Vol. 189, No. 4763 SATURDAY, FEBRUARY 11, 1961 2s. 6d.

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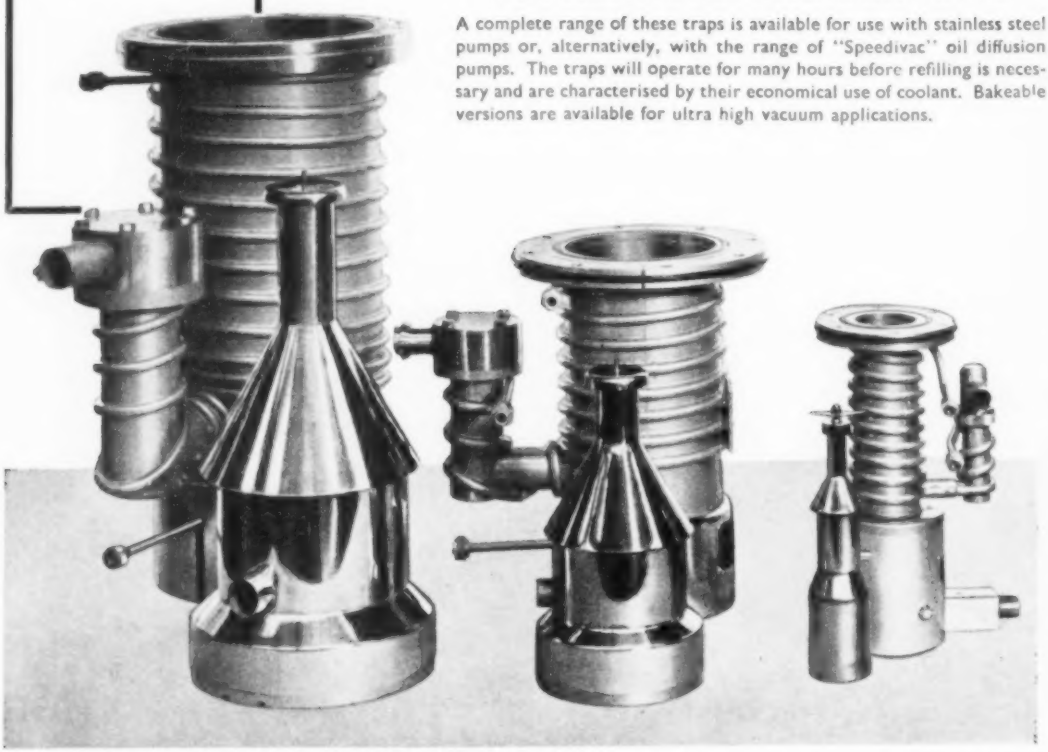

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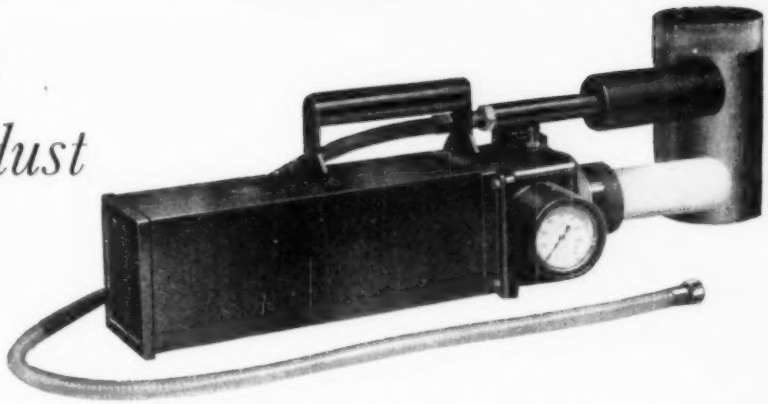

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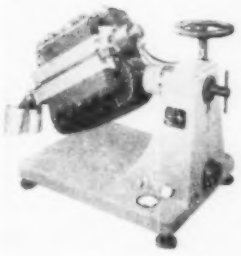

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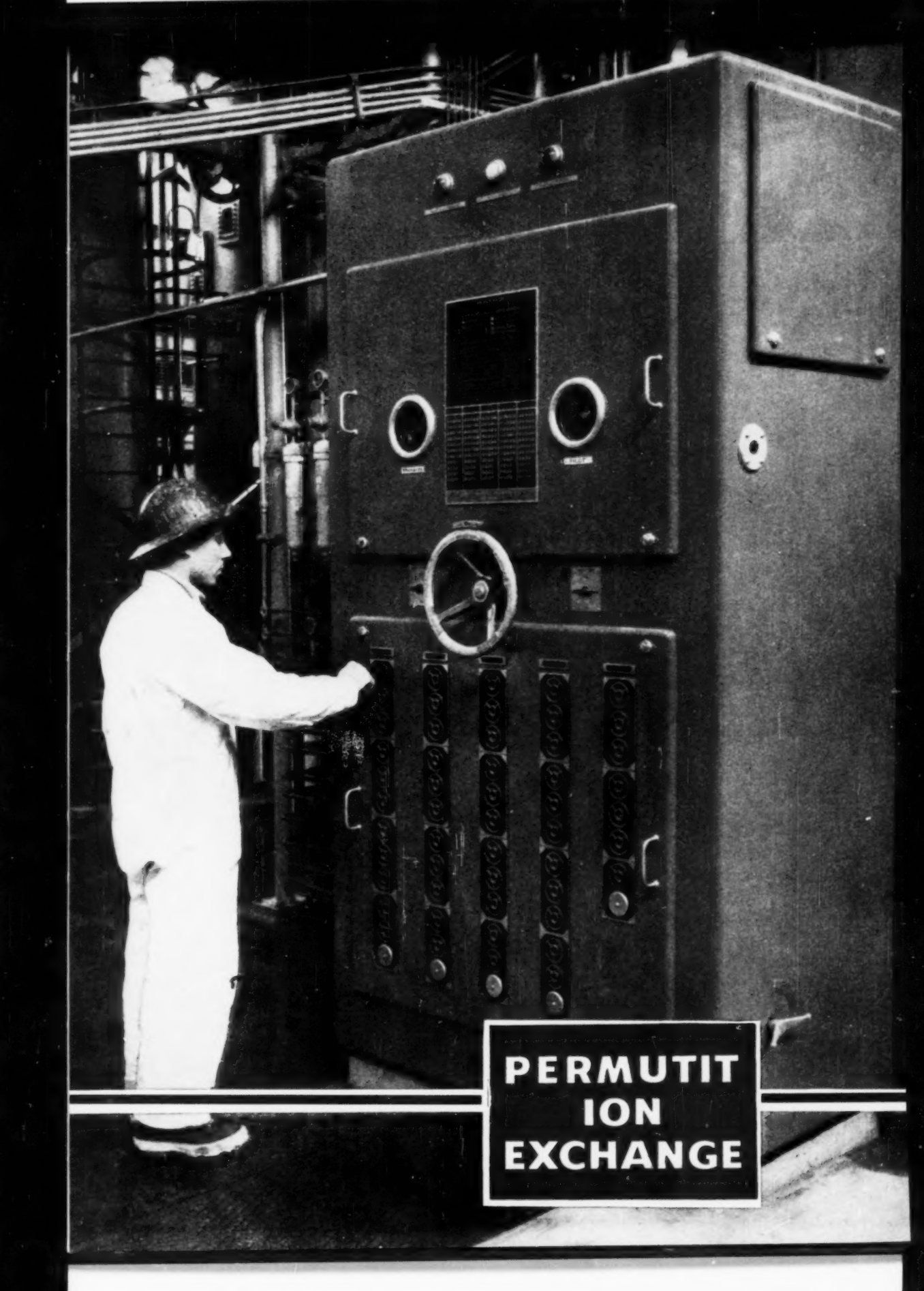
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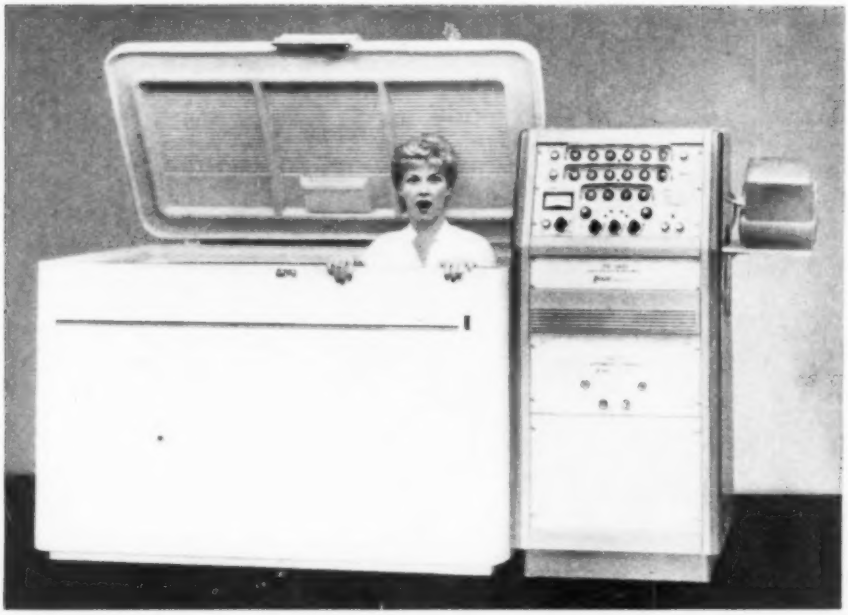

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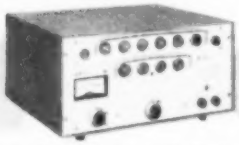

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Autoxidation of Fats

Fats oxidise readily. It is good in a way that they do so for it makes them a useful source of bodily energy. It is not so good in another for it makes them prone to rancidity and other unpalatable oxidative changes. It is important then to try to restrict oxidation to its beneficial role, but one cannot do this effectively without some understanding of the mechanics involved. Early efforts to acquire this understanding culminated in Farmer's hypothesis of a free radical reaction, leading to attack at a methylene group adjacent to a double bond and the formation of a hydroperoxide. Such compounds have since been isolated and identified, in support of the hypothesis. Hydroperoxides are labile substances, however, and in normal circumstances they react further —possibly again by free radical mechanisms— to form either innocuous hydroxy compounds or obnoxious carbonyls. Mechanisms have been postulated, but the conditions under which one or another will operate have not been determined satisfactorily. These are matters of increasing importance in present world economy. Unilever is probably the largest single user of fats so, in Unilever Research, Crossley and his colleagues are working to resolve the problems that remain; studying model systems, relating cause and effect, and establishing conditions for stability of the many types of fats which Unilever use.

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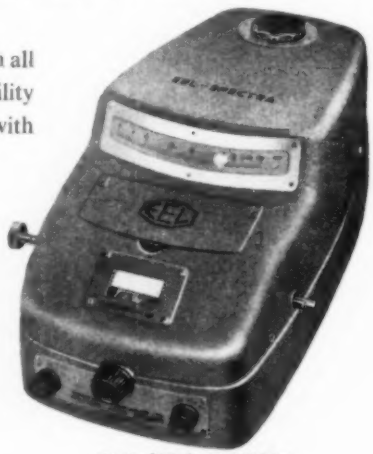

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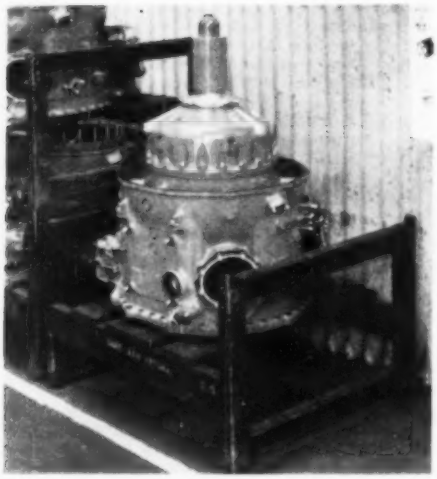

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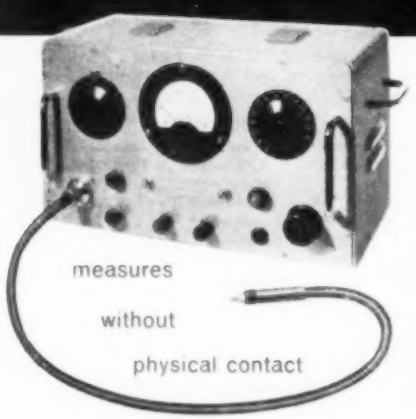

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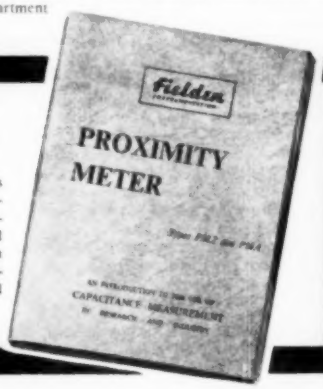

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CONTROL OF UNIVERSITY BUILDING DEVELOPMENT

ON December 20, the Prime Minister announced in the House of Commons that Lord Robbins, professor of economics in the University of London, had accepted the chairmanship of the provisional committee to inquire into higher education in Britain. The full composition of the Committee has not been announced, but its terms of reference were given as follows:

"To review the pattern of full-time higher education in Great Britain and in the light of national needs and resources to advise Her Majesty's Government on what principles its long-term development should be based. In particular, to advise, in the light of these principles, whether there should be any changes in that pattern, whether any new types of institution are desirable and whether any modifications should be made in the present arrangements for planning and co-ordinating the development of the various types of institution."

The long-term development of universities, colleges of advanced technology, certain other colleges of further education and teacher-training colleges, Mr. Macmillan added, would be within these terms of reference. The Government, he said, is trying to get a very broad representation on the Committee and, by doing so, to deal with all the possible groups that should be considered.

These terms of reference clearly permit the Committee to consider the question of university expansion not in isolation but in relation to the educational system as a whole. It could, for example, comment on the merits or demerits of dealing with higher technological education separately from university education, and could probe into the question of relations between the University Grants Committee and the Ministry of Education. It is true that the Robbins Committee is not expected to publish its findings for two or three years, and the University Grants Committee, which is already discussing with the Treasury the increase in non-recurrent grants entailed by university expansion, is expected by this autumn to submit to the Chancellor of the Exchequer its estimate of what the universities will need from Parliament during the next quinquennium—1962–67. The limit to that immediate expansion is likely to be set by the availability of academic staff and capital resources, and the Robbins report should be available when the questions of how far and where the university system should be further expanded, what are its purposes and what should be its relation qualitatively and quantitatively to the educational system of the country as a whole, require decision. Moreover, in the meantime there may be available a good deal of guidance on such matters as curricula, university entrance and the nation's demands for particular categories of trained man-power and woman-power, and supporting auxiliaries.

Two matters that bear closely on the expansion or modification of the university system in relation to national needs have recently received some attention. The first relates to the financial aspect of expansion. When the report of the Gater Committee, which inquired into the methods used by the universities in contracting and in recording and controlling expenditure from non-recurrent grants, was published in 1956, it was contemplated that the application by the universities of the Committee's recommendations would be reviewed at a later date, and in 1959 the University Grants Committee invited Sir Arthur Rucker to undertake this review. Sir Arthur's report has now been published*, and confirms that, with minor exceptions, the procedures recommended by the Gater Committee are being followed. The University Grants Committee accepts Sir Arthur Rucker's recommendations regarding these exceptions, as well as recommendations for further amendments in the procedure both of the universities and of the University Grants Committee itself.

Sir Arthur Rucker emphasizes first both the magnitude of the building programme of the universities seen as a whole and the success already being achieved. As already announced, up to the end of 1963 the programme provides for an increase in student population from 85,000 in 1955–56 to 135,000 in the second half of the 1960's, and if the further expansion to 170,000 already under discussion is realized, the student population of the universities will have been doubled within a relatively short period of years. On January 25, the Chancellor of the Exchequer, in a written answer in the House of Commons, indicated that further expansion had been approved. He had now authorized the University Grants Committee, he stated, to increase the Government-financed university building programmes starting in the calendar years 1962 and 1963 from the present £15 million to £25 million in each year, and for the years 1964 and 1965 he had authorized the Committee to invite the universities to make building plans on a basis of starts of £30 million in each year. The rate at which these plans can be executed must depend on the general state of the national economy and on such factors as building costs; but Mr. Selwyn Lloyd did not anticipate that the figure ultimately authorized would be less than £25 million a year, and he hoped it would be up to £30 million in each year. This large addition to the resources of the universities should, he added, assist materially in the practical task of accommodating the increased numbers of students who would be coming forward in the second half of this decade, and it would be compatible with further development after 1965 to expand the university population to about 170,000 by the early 1970's.

Controversy, occasionally acute, over the merits of individual university buildings, should not be

* University Grants Committee. Methods used by Universities of Contracting and of Recording and Controlling Expenditure. Pp. 28. (Cmnd. 1235.) (London: H.M. Stationery Office, 1960.) 1s. 6d. net.

allowed to obscure the truth that a period of great university expansion is in progress in Britain, and that buildings well suited to its needs will have been provided when the programme of grant-aided buildings has been completed. The real questions are rather where such university expansion should take place, the extent to which such expansion is desirable, particularly in relation to the simultaneous expansion of technological education generally, and to the training of the vastly greater numbers of technicians and craftsmen who are essential if effective use is to be made of the services of the scientists, technologists and other highly trained products of the universities.

All the universities use the Gater Report as their guide in defining the procedures to be used in carrying out their building programme, and for the most part the procedures recommended were already in force. Where this was not so, they have, with a few minor exceptions, been adopted and remain in use. Like the Gater Committee, Sir Arthur Rucker found no evidence that grants-in-aid of 90–100 per cent weakened the sense of financial responsibility on the part of the universities; but there are naturally differences of opinion on the standards and costs appropriate to particular buildings or types of building. It is, however, not always easy to decide the extent to which non-recurrent grants for buildings can or should be supplemented by universities from their own resources. The University Grants Committee has already emphasized the value and importance to university life of the generous gifts which universities receive from foundations, firms and individuals, more particularly as a proof of public confidence in the work which the universities are doing in advancing scientific knowledge and providing the trained man-power on which the future of Great Britain depends; and Sir Arthur points out that, if such gifts are to be encouraged, universities must have a reasonable degree of freedom to spend them in the way which they consider most useful.

Some expenditure and some embarrassment in planning would have been avoided, he notes, if the present targets for expansion could have been fixed at the beginning of the building programme instead of by later increases; but now that all universities have established control procedures on the lines recommended by the Gater Committee, Sir Arthur considers it unnecessary for the University Grants Committee to review in detail the expenditures under minor works allocation: such expenditure should be left to the discretion of the university. Again, he emphasizes the need for great care in examining comparisons of costs, as the costs of university buildings, even when intended for similar purposes, vary widely; and in his view it is in the interest of economy that every reasonable opportunity should be taken to acquire land likely to be needed for development, even when no immediate use is in prospect. An Architect's Division with professional staff has already been created in the office of the University Grants Committee, and with its aid the Committee is seeking to collect information and statistics on all aspects of university building, to examine space requirements and to analyse costs. A beginning has been made with the definition of space standards and limits of costs for various types of university building.

Apart from these general observations, Sir Arthur Rucker is concerned mainly with the application of the recommendations of the Gater Committee. Of even greater interest, however, are the comments which he makes on developments since that Committee reported, and the conclusions and recommendations arising out of those comments. The great expansion of the building programme makes it even more essential that building procedures should provide effective safeguards against waste, extravagance or other abuse; whereas in 1954–55 grants paid for building works amounted to £4,674,545 and for professional fees to £306,242, in 1959–60 the corresponding figures were £13,693,621 and £1,959,775. The Chancellor's statement on January 25 increased this figure of £15 million to £25 million in 1962 and 1963 and probably to £30 million in the following two years. Reference has already been made to the way in which the establishment of an Architect's Division under the University Grants Committee is assisting the collection and analysis of information and statistics relating to university buildings, and the definition of cost limits and space standards; and Sir Arthur's inquiry has confirmed the desirability of defining, so far as this is possible, the appropriate limit of cost for a university building at a very early stage in planning. The special requirements of university buildings must nevertheless not be ignored, and procedures for defining limits of cost must be sufficiently flexible to take account of these requirements.

There are four stages in the present procedures of the University Grants Committee for the approval of building grants, and Sir Arthur recommends that they should be so timed that the second stage—submission of Schedule I—takes place two and a half to three years in advance of the date of giving out to tender. Since the universities were informed in 1958 of the buildings which they could expect to start in each of the years 1960–63, this should now be practicable. He also considers that in so far as it is found possible to define cost limits for university buildings, it should be feasible for the University Grants Committee to simplify the present procedures and normally to dispense with much of the detailed examination of plans and estimates. At present, limits of cost are defined for halls of residence and, in part, for scientific buildings; but particularly in respect of scientific buildings, Sir Arthur again stresses the need for flexibility and taking special circumstances and varying needs into account at all stages of planning.

Sir Arthur Rucker was not concerned with standards themselves, but only with the procedures for their definition and application; but he is concerned

to emphasize that the procedures under which building grants are approved by the University Grants Committee must be devised and applied in close and constant consultation with the universities. This essential consultation would be facilitated, he suggests, if the University Grants Committee were to appoint a Buildings Sub-Committee with membership drawn mainly from the universities. Whatever the arrangements for consultation may be, it is essential that there should be a clear understanding between the members and officers of the University Grants Committee and the universities and their officers at all levels of staffing. If procedures for the control of grant-aided expenditure are to be successful, the present excellent and harmonious relations between the University Grants Committee and the universities must be maintained.

With these concluding words Sir Arthur Rucker endorses, like the Gater Committee, the essential soundness of the present procedures for controlling the expenditure of these large sums of public money, and also, like that Committee, firmly rejects the attack on the system which the Public Accounts Committee maintained for more than a decade. While, however, it is to be hoped that the Public Accounts Committee will not re-open that issue, this further tribute to university administration indicates the outstanding importance of efficient government of universities at the present time, and further, the necessity for securing public understanding of the work which universities are doing and confidence in the ability with which the universities are meeting the demands made upon them. It is clearly within the terms of reference of the Robbins Committee to inquire into the adequacy of the present pattern of university government if it thought fit; but on this second issue, it must suffice to observe here that, while the present arrangements for university administration have come so well out of the searching inquiry to which the Gater Committee and Sir Arthur Rucker have subjected them on the financial side, it is no less important that these arrangements should be adequate to meet the demands which university expansion in Britain is making on them in many other ways.

A UNIFIED TREATMENT OF MODERN OPTICAL THEORY

Principles of Optics

Electromagnetic Theory of Propagation, Interference and Diffraction of Light. By Prof. Max Born and Prof. Emil Wolf. With contributions by A. B. Bhatia, P. C. Clemmow, D. Gabor, A. R. Stokes, A. M. Taylor, P. A. Wayman and W. L. Wilcock. Pp. xxvi+803. (London and New York: Pergamon Press, 1959.) 120s. net.

IT is quite impossible to do justice to a work of such depth and scope as *Principles of Optics* within the confines of an ordinary review; even to list the contents would require several pages. A few general remarks will therefore be made in the hope of tempting any reader who has not already done so to look at a copy for himself as soon as possible.

Perhaps the most striking impression that one obtains is of completeness. The scope is best described in the words of the authors' preface: ". . . our discussion is restricted to those optical phenomena which may be treated in terms of Maxwell's phenomenological theory. This includes all situations in which the atomistic structure of matter plays no decisive part. The connection with atomic physics, quantum mechanics and physiology is indicated only by short references wherever necessary." Within this framework it would be difficult to find any aspect of modern optical knowledge that is not covered. But the impression of completeness extends to the treatment as well as to the subject-matter. Compare for a moment the following three brief extracts. On page 111 the equation:

$$(\text{grad } \mathscr{S})^2 = n^2$$

is derived, n being the refractive index and $\mathscr{S}$ the eikonal, followed by the statement "it is the basic equation of geometrical optics". On p. 163 we read "When the (two thin) lenses are in contact equation ... may be written in the form $P = P_1 + P_2$ so that the power of the combination is then simply equal to the sum of the powers of the two lenses". Finally, on p. 249 we read "In a photographic enlarger ($\varphi \sim 20°$), large sources (frosted bulbs or cold-cathode tubes) often provide reasonably efficient illumination. In a cinematograph projector ($\varphi \sim 5°$) requiring maxium brightness, an electric filament is suitable". It will be seen that the most advanced mathematical treatment, the familiar working formulæ and the practical implications all find a place.

Principles of Optics is valuable as a work of reference; but it may be that its value in showing the interdependence and essential unity of the different approaches may be even greater. Honours students in physics will find here the often-missing links between theoretical and experimental studies. It is interesting to note that even in some of the most mathematical sections the style is clear and vivid. In the early stage of the development from Maxwell's equations we read "Within this layer construct a small near-cylinder bounded by a stockade of normals to T, roofed and floored by small areas δA, . . .". The diagram is almost unnecessary.

Students should be warned, however, that this is emphatically a book for studying rather than reading. The plan of each section is to begin with the most general theory and proceed later to particular practical cases. A certain amount of searching may therefore be necessary to find some of the more familiar material. For example, the chapter entitled "Foundations of Geometrical Optics" begins with the derivation of the eikonal equation already mentioned and we do not meet Snell's law and the elementary laws of reflexion until seventeen pages later.

There have been so many text-books on optics that it is quite thrilling to find so much that is new in both presentation and material in one volume. Its only disturbing feature is that after spending even a very short time in study one is made to realize the vast depth of the subject and the shallowness of one's own understanding of it.

C. A. TAYLOR

THE FOURTH INTERNATIONAL CONGRESS OF BIOCHEMISTRY

Proceedings of the Fourth International Congress of Biochemistry

Vienna, 1–6 September, 1958. Vols. 1–15. (London and New York: Pergamon Press, 1959–1960.) £48 net complete. (Separate volumes range in price, according to size, from 63*s*. to 100*s*.)

THE First International Congress of Biochemistry was organized on the initiative of the Biochemical Society, and was held in Cambridge eleven years ago. There were about 1,700 members and the main publication, apart from a greatly treasured book on Gowland Hopkins, was a volume of abstracts of communications which would almost fit into the pocket. In 1958, the Fourth International Congress was held in Vienna. More than 5,000 attended and the publications of this Congress, now complete, amount to no less than fifteen substantial volumes—well over 4,000 pages in all. It is astonishing that this large bulk of published material should have emanated from the proceedings of a meeting lasting only six days. It is a reminder of the organizing efficiency and hard work of Prof. Hoffmann-Ostenhof (who has also acted as general editor of these volumes) and his colleagues in Vienna, who made it possible for so many communications to be given in so short a time. This meant, of course, that members frequently had to make a choice from among several communications which were being given simultaneously. Now, with the publication of these volumes, they can read what happened at the meetings they had to miss.

The first twelve volumes are devoted to the symposia. It should be stressed that the pre-prints which were made available at the Congress are no substitute for these volumes, which contain revised and much more complete accounts of the meetings. Moreover, they give some account of the discussion which took place. The subjects covered (with volume numbers and editors in parentheses) are the following: (1) carbohydrate chemistry of substances of biological interest (M. L. Wolfrom); (2) biochemistry of wood (K. Kratzl and G. Billek); (3) biochemistry of the central nervous system (F. Brücke); (4) steroids (E. Mosettig); (5) antibiotics (K. H. Spitzy and R. Brunner); (6) biochemistry of morphogenesis (W. J. Nickerson); (7) biochemistry of viruses (E. Broda and W. Frisch-Niggemeyer); (8) proteins (H. Neurath and H. Tuppy); (9) physical chemistry of high polymers of biological interest (O. Kratky); (10) blood-clotting factors (E. Deutsch); (11) vitamin metabolism (H. Molitor and W. Umbreit); (12) biochemistry of insects (L. Levenbook).

The colloquia, dealing with topical questions in biochemistry, are given in Volume 13. They include: sulphur metabolism (edited by K. S. Dodgson); purine and pyrimidine biosynthesis (edited by H. Chantrenne); oxygenating enzymes (edited by O. Hayaishi); metabolism of C_1-compounds in microorganisms (edited by Sir Hans Krebs); biosynthetic mechanisms in higher plants (edited by P. K. Stumpf); and growth chemistry of bacteria (edited by G. Toennies and E. E. Snell). Volume 14 (edited by W. Auerswald and O. Hoffmann-Ostenhof) contains the transactions of the plenary sessions and includes the invitation lectures of the Congress. Prof. E. Chargaff, of New York, lectured on the chemistry of heredity, and Prof. E. Braunstein, of Moscow, on the chemical integration of nitrogen metabolism. Volume 15 consists of abstracts of the sectional papers together with a subject index of the symposia and colloquia, ranging from 'abietic acid' to 'zymosterol'.

The printing, illustrations and binding of these volumes are of high quality. Presumably, most biochemists will have to look to their librarians rather than to themselves to provide the complete set, but fortunately, individual volumes can be bought separately. Whether congress publication can go on increasing in bulk at its present rate, or even be maintained at its present level, is another matter. It might be argued that the amount of material and the cost of its publication are becoming unmanageably large and that, in any event, much of the work will be published in more definitive form in the regular journals. However that may be, to those who were there, these volumes will bring back memories of a week of friendly hospitality in beautiful surroundings—memories, not only of scientific discussions, but also of Mozart's 'Magic Flute' at the Vienna State Opera, and of the first sight of Melk Abbey. All biochemists owe a debt to the organizers of this Congress, and to those who worked afterwards to produce this most impressive permanent record of the meeting.

D. C. Harrison

PROGRESS IN ALKALOID CHEMISTRY

The Alkaloids

Chemistry and Physiology. Edited by R. H. F. Manske. Vol. 6 (Supplement to Volumes 1 and 2). Pp. xii+442. 14 dollars. Vol. 7: Supplement to Volumes 2, 3, 4, and 5. Pp. xiii+558. 17 dollars. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.)

THE arrangement of these volumes follows that of the five original volumes of "Manske-Holmes" which appeared during the period 1949–55, and which these are designed to supplement. The relation of their chapters and sections to the chapters of the original work is carefully detailed, and the numbering in the bibliographies continues from the numbers previously reached. The authorities from Canada, Czechoslovakia, Germany, Hungary, Switzerland, the United Kingdom and the United States are those who contributed the chemical sections of the original, and, like the editor, have lost nothing of their clarity and comprehensive grasp.

The bibliographies may generally be taken to cover as far as 1957, with addenda in one or two cases to 1958. The two volumes may therefore be regarded as an exhaustive review of progress during something less than a decade in alkaloid chemistry.

There is no systematic supplementing of the nine chapters in Volume 5, by specialists on particular pharmacological aspects—among which, even a short time ago, 'tranquillizer' effects found no place—but this omission is to some extent made good by summaries of relevant pharmacological work included in many chapters of the supplement. An attractive example may be noted in section 5 of the chapter on tropane alkaloids, tracing the correlation of mydriatic effects with an esterified α-hydroxyl group on C(3) (as in atropine and hyoscyamine), anæsthetic effects with esters of the stereoisomeric

3β-hydroxyl compounds (in cocaine, tropacocaine and psicaine) and central nervous system stimulation with N'substituents, irrespective of the orientation of the 3-hydroxyl group.

In contrast, the other not strictly chemical topic—that of "Alkaloids in the Plant"—has been so amply supplemented as to extend the bibliography references from 175 to 452; and to the more general reader, this could conceivably prove the most rewarding chapter in the two volumes. It is estimated that about 1,000 naturally occurring vegetable alkaloids have now been characterized, occurring in 10-20 per cent of all plants, and at all levels of the vegetable kingdom, including fungi, lichens and fern-allies. Even these figures may prove a substantial under-estimate if smaller amounts of alkaloids are looked for and recorded; and it may well be the case that there is nothing at all exceptional in the capacity to biosynthesize alkaloids, but only in the capacity to tolerate them in substantial quantities. Thus, in an example quoted, the tomato plant, though itself elaborating small amounts of nicotine, succumbs to the effect of a higher concentration when grafted on to *Nicotiana*.

By the use of radioactive tracers, considerable advances have been possible in knowledge of the site and mechanism of alkaloid biosynthesis. Ring-closure of amino-acids emerges as a widespread pattern, though not always by the most obvious sequence: while the pyrrolidine ring in nicotine, for example, is shown to originate from ornithine, radioactive lysine (the next higher homologue) did not contribute as expected to the pyridine ring, and its radioactivity appeared again in the pyrrolidine nucleus.

Work on variations of alkaloid content due to environmental factors, and to minor genetic differences between geographical races, is rather briefly summarized; and no reference is made to the protracted investigation of these factors in the opium poppy, sponsored by the United Nations to assist in tracing the currents of illicit circulation of opium.

Throughout such botanical-chemical studies, the establishment of a chemical basis for taxonomy remains as a shining objective. The wide distribution with which some alkaloids are now to be credited, however, must be a signal for caution in applying chemical criteria except within narrow and regular taxonomic groups.

Of the original 38 chemical chapters, 30 are now supplemented, affording examples both of swift expansion over new fields, and of the final conquest of ancient peaks previously reconnoitred in long and strenuous approaches. In the former category, most space is claimed by the *Rauwolfia*, *Amaryllis*, *Veratrum* and *Senecio* groups. At the date of the original volumes, knowledge of the *Rauwolfia* alkaloids covered only seven bases of unknown constitution, while from the Amaryllidaceae fifteen were known. From the same sources, the present supplement describes more than forty and more than seventy respectively, the greater number of which are elucidated as to structure, and some of which, including reserpine itself, have been synthesized. Such rapid advances have been mainly made possible by the use of chromatographic techniques for the separation of complex mixtures, and of paper chromatography and infra-red spectra as criteria of a complete separation.

In a comparable way, the use of X-ray crystallography for final confirmation of the structural formulæ, deduced from many years of degradative chemical investigation, may be said to have consolidated the jumping-off ground for the long-awaited syntheses of strychnine, morphine and hyoscine. All these are recorded in the present volumes; and surely it would be a sluggish soul that would find anything out of place when they are chronicled, with a touch of unwonted rhetoric, as a storming of citadels.

E. G. KELLETT

BRITISH DEER FORESTS

The Deer Stalking Grounds of Great Britain and Ireland

Compiled by G. Kenneth Whitehead. Pp. xviii+556+38 illustrations. (London: Hollis and Carter, Ltd., 1960.) 126s. net.

THOUGH the subject has been tackled by three previous writers between 1839 and 1923, this is the first really comprehensive survey of deer forests in the British Isles, and certainly the first with such abundant statistics of the deer bagged. The major part of the book consists of an alphabetical list of deer forests, with the following details: acreage; area above 1,500 ft. and below 1,000 ft., highest and lowest ground; number of deer killed annually, divided into stags and hinds for both pre-1940 and post-war; average weight of stags and hinds, with weight of heaviest stag known to have been killed; and particulars of the most important heads recorded for the forest.

A series of detailed appendixes gives an alphabetical list of the owners of deer forests and shootings in 1959; a counterpart list of the deer forests with their owners; a list of properties of the Forestry Commission in or adjacent to deer-forest country; four different classifications of the best red deer heads recorded in the British Isles during the past 200 years; and a list of the heaviest wild red deer stags known in the same period. The whole is garnished with 38 excellent black-and-white photographs, a dozen useful maps showing the actual location of each forest, a bibliography and several indexes.

It is clear that the sportsman interested in deer-stalking could scarcely expect a more complete provision for his needs. For the naturalist, too, there is an immense amount of valuable material to be quarried from Col. Whitehead's research. Statistical analysis of all these figures about average weights and head sizes surely ought to produce information of much value. There is also a great deal of important information tucked away in the notes that follow the figures about each deer forest, such as when and whence deer have been introduced into them to raise the quality of the native stock, and how these introductions have fared.

Though the great majority of British deer forests are in the Highlands of Scotland, there are also a few in England and Ireland, but none in Wales. The fact that the red deer of Exmoor and the New Forest are hunted with hounds excludes them from consideration, but seven deer forests are listed for the Lake District, while introduced deer have enabled Lundy Island in the Bristol Channel, the Roches in the moorlands of Staffordshire, and Thetford Chase

in the Norfolk Breckland to qualify for inclusion. In Ireland there are ten deer forests, mainly in Counties Donegal, Kerry and Wicklow.

One can have no hesitation in affirming that this very thorough piece of work will hold its own as the standard work on British deer forests until the end of the century, and probably well into the next one as well. But I commend to the Deer Group of the Mammal Society of the British Isles the task of making good use of the vast store of natural history information it contains. R. S. R. Fitter

GEOMORPHOLOGY OF WALES

The Relief and Drainage of Wales

A Study in Geomorphological Development. By Eric H. Brown. Pp. xii + 186 + 24 plates. (Cardiff: University of Wales Press, 1960.) 30*s*.

During the course of the past hundred years a considerable diversity of opinion has accumulated concerning the nature, origin and age of the erosion surfaces in Wales. Many of these views are mutually exclusive. Thus the Permo-Triassic age suggested by O. T. Jones conflicts with Jukes Browne's Cretaceous, and both with W. M. Davis's Tertiary. A. C. Ramsay's submarine hypothesis is in contradiction with W. M. Davis's subaerial argument, and so on. Equally complex is the problem of drainage evolution. T. N. George supports the view of rivers extending their courses across emergent wave-cut platforms of Pliocene age, while A. Strahan has proposed that the new discordant rivers of South Wales have been superimposed from a Cretaceous cover.

The problems of the evolution of drainage and the extent, origin and age of the erosion surfaces are closely linked; these together form the basis of the denudation chronology for any given area. For the first time for Wales these two lines of inquiry are brought together in Dr. Eric Brown's study of the relief and drainage of the whole principality. The survey is thus in the tradition of the classic accounts of the French *Plateau Central*, by Henri Baulig, and *Structure, Surface and Drainage in South East England*, by Profs. Wooldridge and Linton.

This new book is the product of many years of study and much field work, and gives for the first time a systematic geomorphological account of much of the landscape of Wales. Although some of the conclusions advanced by Dr. Brown are open to discussion, all those interested will applaud his introductory survey of the relief and structure of Wales and his masterly account of the views put forward during the past hundred years to account for these features.

In the second half of the book Dr. Brown advances his own interpretation of the denudation chronology in considerable detail. Evidence is submitted for the existence of at least three high-level subaerial peneplains of early Tertiary age above 700 ft.: and below this height for a series of coastal plateaux, notably at 600-, 400-, 300- and 200-ft. levels, of submarine origin and Pleistocene age. The drainage evolution is worked out in relation to these erosion surfaces. Forty-seven maps and diagrams and twenty-four plates support the text, and the account concludes with a comprehensive bibliography.

The bibliography will be of great value to future research workers in this field, but it is perhaps unfortunate that there is no reference to Dr. Brown's paper on "The Physique of Wales" given to the Royal Geographical Society on October 29, 1956 (*Geographical Journal*, **123**, Part 2, June 1957). This paper is of great interest and value, as the nature and extent of the problems still outstanding after Dr. Brown's analysis and synthesis of the geomorphology of Wales clearly emerge in the discussion which followed. One other addition to the book might have been considered—a short glossary of Welsh landscape terms. So many Welsh place names arise from the topography that additional interest would doubtless be added for the English reader if an indication of the meanings were made available.

W. G. V. Balchin

INTRODUCING METEORITICS

Principles of Meteoritics

By E. L. Krinov. Translated from the Russian by Irene Vidziunas. Translation edited by Harrison Brown. (International Series of Monographs on Earth Sciences, Vol. 7.) Pp. xi + 535 + 7 plates. (London and New York: Pergamon Press, 1960.) 70*s*. net.

The original edition of Krinov's introductory book on the study of meteorites has been available in Western meteorite laboratories for some years, but it is doubtful whether many investigators have actually read more than the sections of particular interest to their own work. It is essentially an introductory text, and, as such, may be read with profit by the sort of informed lay public at which Sir Lazarus Fletcher's British Museum guide was directed; but there is also included a section on the external appearance of fusion crusts which represents an important original contribution to the subject by the author himself. D. R. Chapman's recent article on tektites (*Nature*, **188**, 353; 1960) indicates how profitably such work may be extended by aerodynamicists.

The treatment is naturally from a Russian point of view, and most of the specialist articles quoted are of Russian origin, but a real effort was made in the original edition to acknowledge the importance of work by Prior and Hey, Perry, Urey and others. The translated version also includes a selection of both Russian and American work published since the original edition.

In so far as I am able to check it, the translation appears very faithful. In the original, the text and legend are at one in their misinterpretation of Fig. 121, whereas in the translation the text follows the original, but the legend (Fig. 129 of the translation) has been altered to a factually correct form.

Several additional illustrations have been incorporated in the translated edition, and some of the original illustrations have been replaced by more up-to-date or clearer ones. In a work of this nature the half-tone illustrations are of great importance, and it is very unfortunate that in reproduction some of them have deteriorated. On the other hand most, but not all, of the new illustrations are of good quality. A very serious loss in the translated edition is the totally inadequate version of Fig. 52, but this could easily be corrected. H. J. Axon

Vistas in Free-Radical Chemistry

Edited by Dr. W. A. Waters. (International Series of Monographs on Organic Chemistry, Vol. 1. Supplement No. 3 to *Tetrahedron*). Pp. ix+251. (London and New York: Pergamon Press, 1959.) 75*s*. net.

THIS book is published in memory of Dr. Morris S. Kharasch, and is a fitting tribute to one of the great organic chemists of this century. A complete list of the published papers of Kharasch and his collaborators is given, and is followed by a selection of twelve papers which are presented in full; these include descriptions of Kharasch's early work on the discovery and exploitation of the 'peroxide effect' and some recent work on polymerization reactions. Many of us have a lesson to learn from Kharasch's attention to detail, which has led to several important discoveries. F. R. Mayo and C. Walling pay personal tributes to Kharasch, and give very interesting accounts of their work in collaboration with him. An account of modern work and trends in free-radical reactions in solution is given by W. A. Waters.

The book concludes with chapters on homolytic aliphatic and homolytic aromatic substitution, by H. C. Brown and D. H. Hey, and some other aspects of free-radical chemistry, including a concise account of free-radical reactions in gases by K. O. Kutschke and E. W. R. Steacie. The object of including these chapters is to illustrate the effect of Kharasch's research on the development of free-radical chemistry; this is now such a large subject that a comprehensive treatment would not be possible in only 250 pages. The aspects selected will be, on the whole, of interest to organic chemists, particularly those working on free-radical reactions.

The volume is a useful historic record of Kharasch's contribution to free-radical reactions in solution.

A. B. Callear

Public Relations and Management

By David Finn. (Reinhold Management Science Series.) Pp. xiii+175. (New York: Reinhold Publishing Corporation; London: Chapman and Hall, Ltd., 1960.) 36*s*. net.

SUSPICION of those who court publicity has led the British people to look askance at men and women who act as public relations officers for their organizations. This suspicion has been strengthened by some of the public relations practitioners whose efforts to influence the Press have been, to say the least, somewhat unsavoury.

Against this canvas, genuine public relations officers have had difficulty in establishing themselves and, particularly, in showing that their jobs consist of considerably more than preparing hand-outs for the Press. Yet many companies are becoming aware that it is not enough to provide needed goods and services for the community: to obtain maximum results the company must present an image to the public which will persuade more and more people to make use of those goods and services. The public relations officer is concerned to influence public opinion favourably towards his company.

David Finn is an experienced public relations consultant in the United States and, in this book, does much to show the worth of effective public relations to a company. He strips the gloss from the brassy publicity-seeking public relations officer, and illustrates how the practitioner can create a favourable climate of opinion for his company by examining every corporate act to see what effect it will have on public opinion and how projects should be designed to win public support. Besides managing directors, this modest, well-reasoned case should appeal to many heads of institutions outside the world of industry.

T. H. Hawkins

Homotopy Theory

By Sze-Tsen Hu. (Pure and Applied Mathematics, Vol. 8.) Pp. xiii+347. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959.) 11 dollars.

A COMPREHENSIVE introductory account of the rapidly growing field of homotopy theory is welcome; the present volume is rather less concise than Hilton's Cambridge Tract, and differs from it somewhat in content. It is not altogether easy reading, and a really sound knowledge of elementary algebraic topology is an essential preliminary. The main problem in homotopy theory is the extension problem studied in Chapters 1 and 2; fibre spaces and mapping spaces fill Chapter 3. The next four chapters deal mainly with homotopy groups and cohomotopy groups, and the final group of four chapters is concerned chiefly with spectral homology theory. Specialists in a domain which is expanding so quickly may quarrel with some of the omissions; but the young topologist must be grateful for so well-balanced and clear an account. There are exercises to each chapter, but the reader must be warned that these range from the trivial to the impossible, the latter being those which merely summarize results to be found in the periodical literature of the subject; a clear separation between genuine exercises and bibliographical annotations might have been a better plan.

T. A. A. Broadbent

Dictionary of Nutrition and Food Technology

By Dr. Arnold E. Bender. Pp. vii+143. (London: Butterworths Scientific Publications, 1960.) 30*s*.

DR. BENDER'S *Dictionary* sets out to interpret the technical terms used by the many different scientific and practical groups who take part in the expanding knowledge of nutrition. Practical workers in food technology may well be lost in the jargon of the biochemist, while the scientific workers may need definition of technological terms. The dictionary covers the most common biochemical, bacteriological, chemical and technological processes in food science, with brief descriptions also of equipment used in the laboratory and in manufacturing processes.

The sources of information listed in the introduction to the dictionary provide a useful nutrition bibliography, although there are some serious omissions, such as the failure to give full references for the publications of the U.S. National Research Council and the Nutrition Committee of the British Medical Association. Some of the information on special diets is not from the most up-to-date sources and some misleading statements, such as the correlation of glossitis with ariboflavinosis, need to be corrected. The choice of foods for which composition figures are given seems rather arbitrary, and the sources of the food analyses need some further explanation. However, in spite of such flaws, the dictionary is a useful addition to the nutrition bookshelf and should solve many questions of terminology.

A. M. Copping

AUSTRALIAN UNIVERSITIES

By Sir ERIC ASHBY

Clare College, Cambridge ; formerly Professor of Botany, University of Sydney

IN 1957, a Committee appointed by the Prime Minister of Australia, under the chairmanship of Sir Keith Murray (chairman of the University Grants Committee in Great Britain), issued a report which has brightened the prospect for Australian universities. One outcome of the Murray Report was the creation of an Australian Universities Commission, which consists of five members : a full-time chairman (Sir Leslie Martin, formerly professor of physics in the University of Melbourne), two members drawn from academic life, and two from industry.

The Commission has presented its first Report*. This summarizes the development of the universities over the triennium 1958–60 in student-numbers, staff and finance. It then goes on to set out the Commission's recommendations for the triennium 1961–63 ; and it has chapters on halls of residence and on the future of Australian universities.

It is a record of remarkably rapid expansion since the date of the Murray Report, and a prediction of further rapid expansion over the next three years. The following figures (selected from tables in the Report) illustrate the rate of growth of Australian universities :

	1950	1952	1960
Enrolments	—	27,325	53,478
Academic staff (State universities)	—	1,645	2,972
Recurrent income (£1,000)	3,756	—	22,677

The figures for enrolments indicate that nearly 6 per cent of the 17–22-year-old age group are enrolled at universities ; but the figures have to be interpreted with caution, for only 32,349 of the enrolled students (60·5 per cent) are attending universities full time. No fewer than 15,997 students (29·9 per cent) are taking part-time courses and 5,132 students (9·6 per cent) are external. The figure, therefore, which is comparable with those published by the British University Grants Committee is 32,349 full-time students in 1960. Even so, Australia already has a somewhat higher proportion of her young people at universities than Great Britain has.

The figures for numbers of academic staff also have to be interpreted with caution, for it is characteristic of State universities in Australia that great use is made of part-time staff. However, when the figures for enrolments and for academic staff are adjusted to take account of the fact that there are part-timers in both categories, the student-staff ratio comes out at about 14 : 1, compared with an average for British universities of about 9 : 1, and for American universities, colleges and junior colleges of 13 : 1.

The figures for recurrent income reflect first of all Commonwealth participation in university finance (an increase from £0·388 million in 1950 to £7·610 million in 1960), together with substantial increases in grants from State Governments (from £1·616 million in 1950 to £8·727 million in 1960) and in student fees (from £0·697 million in 1950 to £3·039 million in 1960). It is noteworthy that this fee-income is about the same as the income from fees from 63,068 full-time students in eighteen English universities and colleges in 1954–55.

Notwithstanding the recent rapid expansion of Australian universities, the Commission sees no alternative ahead but further rapid expansion. The Report predicts that by 1966 there will be at least 95,000 students enrolled in Australia's ten universities. It is estimated that the University of Sydney alone will have 16,300 students and the University of Queensland 18,000.

The Commission does not disguise the fact that this immense increase in enrolments will precipitate problems both of standards and of staff. Already such data as are available indicate that fewer than half the students at Australian universities graduate in the minimum time. The Commission does not recommend a stiffening of the standards for entrance to universities, nor an increase in maturity of freshmen (which could be secured by raising the age of entry to universities). So as numbers increase the prospect is that student-performance will deteriorate rather than improve.

This possible deterioration might be corrected by a very substantial improvement of the student-staff ratio (though there is no convincing evidence to support this belief). The Commission estimates that 3,613 university teachers, over and above the present numbers (an increase of more than 100 per cent), will be needed by 1966. To recruit academic staff in these numbers is the most perplexing problem facing the universities of Australia.

Comparisons of costs between British and Australian universities are very difficult to make, and the figures given in the Report (£A.448 per student in Australian State universities compared with £A.562 per student in eight 'representative' British universities) should not be compared without qualifications. The case, however, for increased grants to Australian universities needs no such comparison to support it. After surveying the needs of the universities in detail the Commission makes the following recommendations for the triennium 1961–63. The figures are in millions of pounds (Australian).

	Commonwealth share	State share
State universities		
Recurrent (spread over 1961–63)	25·424	47·040
Capital (including building, furnishings and equipment, 1961–63)	15·385	15·385
Total (1961–63)	40·809	62·425
Australian National University		
Recurrent (spread over 1961–63)	9·250	—
Capital (including building, furnishings and equipment, 1961–63)	5·156	—
Total (1961–63)	14·406	—

* Report of the Australian Universities Commission on Australian Universities 1958–1963. Pp. vi+77. (Commonwealth Government Printer, Canberra, 1960.)

If these recommendations are accepted the overall expenditure on universities from Government sources (both State and Commonwealth) in the triennium 1961–63 will be nearly £118 million.

In commenting on the prospect which confronts higher education in Australia, the Commission encourages universities to explore fresh ways to make the best use of their available accommodation and high-level man-power. It mentions a submission received from Prof. H. C. Webster in Queensland, outlining a revision of the university calendar which would lead to doubling of utilization of lecture rooms and laboratories, and an experiment already operating in the University of Pittsburgh which allows some students to spend eleven months instead of nine each year on formal academic work. The Commission also suggests that some consideration might be given to the creation of 'satellite' colleges, associated with parent universities, for first-year students. Australia already has experience of this, for the University of Melbourne set up a temporary first-year college near Mildura at the end of the Second World War. It is clear from a reading of the Commission's Report that the Australian universities, which in their constitution and administration are modelled on Scottish universities, have reached a critical stage of their history. Their size has already outgrown their structure. The Commission is evidently giving very careful thought to their future, and is encouraging the universities to propose solutions to the problems which confront them.

PSYCHOLOGY AND THE INDIVIDUAL

By G. W. H. LEYTHAM

Department of Psychology, University of Liverpool

MORE than a hundred years ago, John Stuart Mill differentiated between Psychology, the science of mind, and Ethology, the science of character: "The one ascertains the simple laws of Mind in general, the other traces their operation in complex combinations of circumstances. Ethology stands to Psychology in a relation very similar to that in which the various branches of natural philosophy stand to mechanics. . . . Ethology, the deductive science, is a system of corrolaries from Psychology, the experimental science". ("A System of Logic", 1843.)

The development of psychology has been fraught with dichotomies of this kind, but their proponents have usually been much more partisan than was Mill, and they have been more inclined to regard the two views as being in conflict rather than as complementary. While the academic Wundt was founding the first psychological laboratory at Leipzig in 1879, for the study of the generalized, adult, human mind, Charcot, the medical therapist, was busy in Paris studying the effects of hypnosis on mental patients. The former led to experimental psychology and schools, such as Structuralism, Gestalt and Behaviourism, while the latter paved the way for Freud's psychoanalysis and the divergent theories of Jung and Adler.

Already, in 1894, the German philosopher Dilthey was objecting to the narrowness of experimental psychology, with its explanation and analysis (*Erklärende Psychologie*) and its use of the techniques of natural science (*Naturwissenschaft*). He wanted psychology to study character or human values and to be concerned with understanding and description (*Verstehende Psychologie*). The individual was to occupy a central place in this approach, and psychology would thus serve as a basis for the cultural and social sciences (*Geisteswissenschaft*). In the same year, another philosopher, Windelband, characterized the two approaches as the 'nomothetic' and 'idiographic' respectively. He also felt that the latter was truly scientific, and should be the method followed by psychology.

This distinction between the search for general laws and a concern for the uniqueness of the individual has since shown itself in the gulf which has at times separated the experimentalist from the clinician, the psychologist from the psychiatrist, and, in a wider sense, the pure or theoretical scientist from the applied or practical scientist. It can even be seen in the gap between the sciences and the arts, but in none of these is it necessary or desirable: the aims of the two approaches are different but not antagonistic. Mill said that: "Art in general, consists of the truths of Science, arranged in the most convenient order for practice, instead of the order which is most convenient for thought," and according to his definition, ethology was "the science which corresponds to the art of education; in the widest sense of the term, including the formation of national character as well as individual".

In his presidential address to the British Psychological Society in 1958, Rodger spoke about "Psychologists: Non-medical and Medical"[1], and discerned at least three dichotomies in the history of psychology: cognitive versus non-cognitive (what is studied); experimental versus non-experimental (how it is studied); and laboratory versus extra-laboratory (where it is studied). He pointed out that those working in one 'cube', for example, carrying out experiments in the laboratory on cognitive processes, should realize that theirs was only one room in a large house, and that they should not ignore or belittle the work going on in the other and more distant ones, for example, observations of neurotic behaviour made in the clinic.

The conciliatory nature of Rodger's address may well be taken as a sign of the times, for there are encouraging indications that as psychology emerges from its reviewing phase, it is inclining away from the old theses and antitheses towards a new synthesis. Take, for example, the series of papers on modern trends in psychology[2] read at the annual conference of the British Psychological Society in 1960. The first was concerned with "perception and information theory" and indicated some of the ways in which the mathematical theory of communication deriving from Shannon and Weaver (1949) could be applied to perceptual data. In this approach, the limitations of which are noted, the stimuli are

regarded as 'input', the subject as a 'communication channel', and responses as 'output'. The paper on behaviour theory pointed out that the large-scale, controversial theories, such as those of Tolman and Hull, were going out of fashion and were being replaced by an emphasis on fact finding and the construction of mathematical models based on a probabilistic conception of behavioural processes. Models using concepts from electronics or communication engineering, and having an obvious connexion with cybernetics (Wiener, 1947), were also being used. The contribution on social psychology welcomed the rapidly diminishing use of stimulus-response language in that field, and noted an increased stress on human interaction and language. One systematic approach to the former owed much to the theory of games, while the latter could be studied in terms of information theory, or as an important aspect of the sorts of constructs a person builds up to make his world more predictable, and to use in identifying and evaluating his social environment.

In the remaining paper, on thinking, Allport is quoted as saying that our entire mental life is dominated by a process whereby experiences are formed into clusters, concepts, or categories. While this interest in concept formation and language obviously relates the psychology of thinking to social psychology, one can also see affinities with the other two fields already mentioned: current research in thinking is largely exploratory, and some of it stems from analogies drawn between thinking and information-processing computers. The use of probabilistic inference in the solving of syllogisms has also been investigated. The kind of strategy a person will use to solve a problem seems to depend largely on his previous experience; hence there is also a connexion with personality studies and with a consideration of the individual.

Perhaps this fresh impetus in the long-neglected study of human thinking and language will hasten the reconciliation of the nomothetic and idiographic approaches and bring us nearer to the day when the truly complementary nature of Mill's two sciences will be realized. This would also seem to be the opinion of Hearnshaw who, in his presidential address to the British Psychological Society in 1956[3], spoke of the tension "between the demands of scientific method and the appreciation of the richness of human individuality". He said: "I can see only one way of narrowing the gap between the scientific and humanistic psychologies, and that is through a gradual encroachment of scientific techniques upon territory already roughly mapped by humanistic insight. This means in effect a constant search for concepts which, while capable of scientific definition and employment, nevertheless possess humanistic implications in the sense that they throw light upon peculiar, or, as they are sometimes termed, the higher attributes of men". His own interest in the psychology of thinking has centred around temporal integration, which he regards as one such bridging concept.

Allport, in his book "Becoming" (1955), considered that: "Virtually all modern psychological theories seem oriented toward one of two polar conceptions . . . the Lockean and the Leibnitzian traditions respectively". Whether this be regarded as a dichotomy or a continuum, it can be seen to be very much in line with the scientific–humanistic conflict inherent in the other pairs of opposites. At the Lockean end, man is a *tabula rasa* reacting to external forces, while at the Leibnitzian end, he is the monadic source of all his behaviour. Put in these extreme forms, the inadequacy of either taken by itself becomes obvious, and one can see that although some theories in psychology are presented as if they accounted for the whole of man's behaviour, they do in fact only refer to part of it. Many theories are thus mutually exclusive rather than contradictory, and complementary rather than in conflict. Allport felt, however, that psychologists had tended to concentrate too much on the lower end of the scale, and he called for further scientific studies of the later and higher levels of development, including growth, adulthood, and man's religious sentiment. Such investigations would serve to augment many already carried out on rats, children and neurotics, and as he saw it: "The major task of psychology to-day is to enlarge its horizons without sacrificing its gains".

Several straws in the wind suggest that Allport's dictum is being taken seriously, for apart from the renewed interest in the psychology of thinking mentioned above, the study of mature people made by Maslow, and reported in his book, "Motivation and Personality" (1954), has opened up a new field of inquiry, and the numbers interested in psychological health and the potential greatness of man has grown so rapidly that a new periodical, *The Journal of Humanistic Psychology*, is to start publication very shortly. The new American *Journal of Existential Psychiatry* also provides a forum for those who wish to "help shape the picture of an organism at once mechanical and random, statistical and individual, limited and free", and is evidence of the increasing rapprochment between the humanized behaviourism of the United States and the Continental stress on man-in-action and phenomenology.

The recent "Handbook of Aging and the Individual" (1959), edited by J. E. Birren, reveals a growing interest in adulthood and old age, and the study of human phenomena not at the moment susceptible to high levels of numerical description has been greatly facilitated by the appearance of Siegel's "Non-parametric Statistics for the Behavioral Sciences" (1956).

A pioneering study by Harlow on "The Nature of Love"[4] has shown how problems of the clinic and everyday life can be investigated experimentally in the laboratory, and serves to emphasize that techniques are of secondary importance. Provided he asks worthwhile questions, the psychologist has no need to apologize because his laboratory does not resemble a real-life situation. A vacuum is scarcely representative of the physical world, yet Lord Kelvin once said that we knew more about a vacuum than we knew about anything else. As, in going from a vacuum to the everyday physical world, allowance must be made for the properties of the particular object and the forces acting on it, so, in going from the laboratory to the everyday psychological world, we must allow for the heredity and experiences of the particular individual and the psychological forces present in his environment. Presumably this is what Mill meant when he said that psychology was the science of the elementary laws of the mind and ethology "the subordinate science which determines the kind of character produced, in conformity to those general laws, by any set of circumstances, physical and moral".

Einstein said: "The object of all science, whether natural science or psychology, is to coordinate our

experiences and to bring them into a logical system". ("The Meaning of Relativity", p. 1.) The experiences of psychologists have been so diverse that one would expect their logical systems to be varied too. Observations of the behaviour of rats running in mazes may well lead to a theory quite different from one based on listening to the free-associations of neurotics lying on couches. These are complementary theories, however, and not alternatives: each is limited and applies to a different situation.

The big need in psychology to-day is for a conceptual framework in which all the experiences and theories can be related to each other. We have theories for many of the bits, but so far there is no satisfactory theory of the whole. Such a theory would not only have to bring together and relate the various aspects of behaviour, but would also have to take account of the fact that development and growth are psychological as well as biological.

As a first step in this direction, it would be helpful to have an agreed unit for the science of psychology. The most obvious and useful one is that of the individual, but although lip-service is often paid to this it is frequently reduced to a physiological organism or an inanimate machine, and is rarely described in psychological terms derived from a consideration of the integral and extensive nature of its behaviour. In an attempt to establish the individual as the unit of psychology, I would like to introduce a model of it which I have been developing over the past few years, and which I have found helpful as an integrating framework.

A diagram of the structure of the individual is given in Fig. 1, and although a detailed description of its dynamics is not possible here, it is hoped that the following summary will give some idea of its possibilities in expediting the above-mentioned trends towards the extension and unification of psychology.

Introductory text-books in psychology seem to have grown by accretion rather than by design, and there is a certain autonomy about their chapters which makes it difficult to appreciate the essential unity of the individual's behaviour. How would the proposed model cover the topics of the various chapters and help to bring them together into a unified whole?

The social, physical and biological environments impinge on the individual at the nucleus, which is both a transformer and a relay station: it transforms incoming stimuli and relays them to the ego and also receives outgoing stimuli from the ego and transforms them into action or responses. Psychologists studying the relationship between the behaviour of the psychological individual and the activities of the biological organism, or with the machine-like aspects of behaviour, would be concerned mainly with the properties and functions of the nucleus. Those interested in problems of sensation would find the physical level of awareness and its relation to the nucleus relevant to their work. Feeling and emotion would, of course, have special reference to the emotional level of awareness, while reasoning and other activities involving the use of language would come within the sphere of the mental level of awareness. Certain aspects of creative thinking and the higher forms of religious experience would be referred to the intuitive level of awareness.

The ego can operate on any level of awareness and represents immediate experience or the perceptual world, from which the social, physical and biological worlds are inferred. Problems of perception would thus relate to the dynamics of the ego and the particular level of awareness on which it was functioning. Learning would also apply to all levels, and it seems likely that psychological time (the 'specious present') would correspond with increasing spans of physical time at successive levels of awareness away from the nucleus.

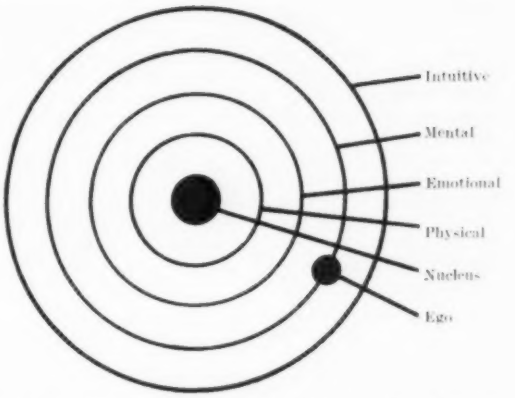

Fig. 1. A model of the individual, showing the four levels of awareness, the fixed nucleus, and the mobile ego

The successive levels of awareness are also related to the successive stages in psychological development, and these may be understood with reference to the range and preferred focus of ego functioning. The model accords well with Maslow's theory of motivation, which states that "the basic human needs are organized into a hierarchy of relative prepotency". As a 'lower' need becomes satisfied, or assured of satisfaction, so the next 'higher' need emerges and becomes central in guiding behaviour. Maslow's hierarchy of needs, together with the aspect of the model of the individual to which they seem relevant, are as follows: physiological needs (nucleus); safety needs (physical level of awareness); belongingness and love needs (emotional level of awareness); the esteem needs (mental level of awareness); and the need for self-actualization (intuitive level of awareness).

It will be seen that Jung's four functions—sensation, feeling, thinking and intuition—also bear a close resemblance to the four levels of awareness. So far as possible, static terms such as 'the unconscious' would be avoided in this model and would be replaced by dynamic relationships, for example, relative availability to the ego as determined by comparative thresholds of arousal.

As we come to know more about the unity of the individual and the way in which its different parts are integrated to function harmoniously, so may we come to understand not only optimal psychological growth, but also disintegration and disharmony. A useful model would thus help us to ask the right questions and guide our search for fresh facts, as well as enhancing the value of the facts already known by bringing them together and relating them in a dynamic system.

How would the suggested model help to bridge the gap between the pure and applied fields of psychology? The structure and dynamics of the abstract, theoretical individual, would be the concern of the pure scientists, while the application of the

generalities thus found to the life and experiences of the particular individual in his particular situation would constitute the aims of the applied psychologists. Knowledge obtained in this latter field would be 'fed back' to the theorists and experimentalists to help them in the modification of their model and in the formulation of vital problems for research. The two aspects of psychology would thus be complementary and mutually helpful, and the answer to the question implied in the title of Lafitte's book, "The Person in Psychology: Reality or Abstraction" (1957), would be 'both': reality in applied psychology, and abstraction in pure or theoretical psychology.

I have tried to show that the time now seems ripe for an attempt to integrate and unify the many facets of psychology, and have proposed a model of the individual as a contribution towards this. Should it prove helpful to psychologists as a logical system whereby they can co-ordinate their experiences, then the similarity between its structure and those of the atom and the solar system may also take us a step nearer to that more distant goal of the unification of all science.

[1] Rodger, A., *Bull. Brit. Psychol. Soc.*, No. 36, 1 (1958).
[2] *Bull. Brit. Psychol. Soc.*, No. 42, 23 (1960).
[3] Hearnshaw, L. S., *Bull. Brit. Psychol. Soc.*, No. 30, 1 (1956).
[4] Harlow, H. F., *Amer. Psychologist*, **13**, 673 (1958).

THE COSMIC RAY FLARE ON NOVEMBER 12, 1960, AND SOLAR ACTIVITY DURING THE PERIOD NOVEMBER 10–15, 1960

By STAFF OF THE IONOSPHERE AND RADIO-ASTRONOMY SECTION OF THE NETHERLANDS POSTAL AND TELECOMMUNICATIONS SERVICES

THE region of solar activity which passed the central meridian on November 12, 1960, at heliographic latitude 27° N. produced a remarkable series of flares, two of which caused cosmic-ray effects at ground-level. In this communication we give a short account of the optical, radio-astronomical, cosmic-ray and earth-current observations made at the Nera Observatory of the Netherlands Postal and Telecommunications Services and at the observing stations at Paramaribo (Surinam) and Hollandia (New Guinea).

The principal flare events belonging to this series are summarized in Table 1.

The radio responses associated with these flares were all spectral type IV, consisting of prolonged continuum radiation on both centimetre and metre wave-lengths. The durations listed for 200 Mc./s. in Table 1 apply to the main part of the events only. After the flare of November 10, radio noise at this frequency continued to be enhanced up to the early hours of November 13. Initially this enhanced radiation showed relatively little variability, but on November 12 strong activity of type I storm-bursts developed. The flares of November 14 and 15, on the other hand, did not provoke prolonged enhanced or storm radiation.

The flare of November 12 is comparable in importance to that of the famous cosmic ray flare of February 23, 1956. Some of the features of this event will be described here.

Optical Development

Fig. 1 shows some photographs in H_α light of this flare taken at Nera. Notable features of this phenomenon are the following: (1) the undulatory structure of the north-eastern branch (the upper branch in Fig. 1) which was especially pronounced at about 1328 U.T.; (2) the very bright portions between the two big spots and the conspicuous bright knot on the northern side; (3) the very rapid extension of the flare in the south-westerly direction between 13h. 27·5m. and 13h. 28·5m.; (4) the coverage of the nearby spots by luminous material around 1334 U.T.

Table 1. Important Flare Events belonging to the Activity Region with CMP on November 12, 1960
(9,400 Mc./s. data taken from Japanese Ursigram information)

Date	Optical flare		Radio response				Geomagnetic activity
	Position	Importance	Frequency (Mc./s.)	Start, time (U.T.)	Duration (min.)	Integrated flux density (10^{-19} × W.m.$^{-2}$ (c./s.)$^{-1}$ min.)	
November 10	28° E. 29° N.	3	2,980	1119	33	1,200	
			545	1116	28	4	
			200	1116	44	500	
,, 11	— —	—	9,400	0311	104	—	
			545	0318	160	320	
			200	0321	250	700	
,, 12	2° W. 27° N.	3 + (C.R.)	2,980	1322	100	34,000	SSC 1348 U.T. (storm: 1710 →) si 1022
			545	1327	100	100?	
			200	1327	270	80	
,, 13							
,, 14	20° W. 28° N.	2 +	9,400	0336	—	—	
			545	0335	120	12	
			200	0319	140	15	
,, 15	32° W. 30° N.	3 + (C.R.)	9,400	0217	41	—	SSC 1303 storm: 2202 →
			545	0221	160	10	
			200	0221	238	40	

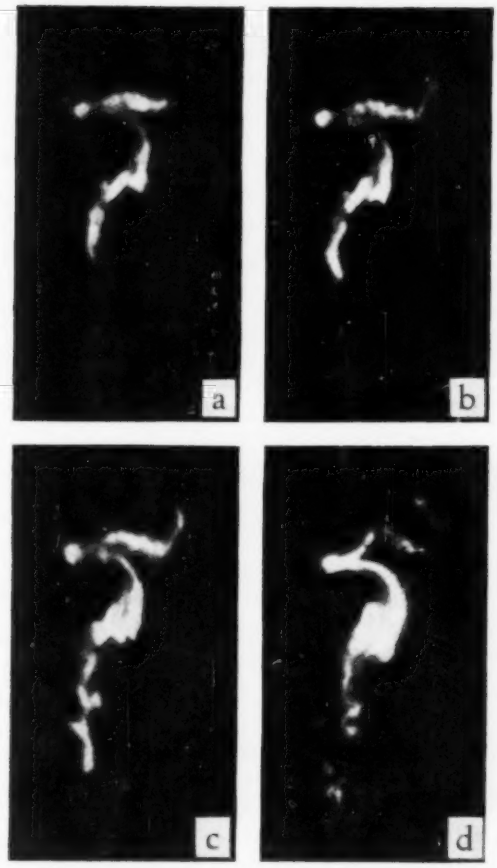

Fig. 1. Photograph in H_α radiation of the flare of November 12. (*a*) 13h. 27m. U.T.; (*b*) 13h. 27·5m. U.T.; (*c*) 13h. 28·5m. U.T.; (*d*) 13h. 34m. U.T.

The overall structure of this flare was very much the same as the structure of a flare earlier in the day, observed at 1012 U.T. at the same position. These two flares illustrate nicely the well-known fact that flares within the same region of activity tend to recur along similar structural patterns.

Radio Responses

A small initial rise at frequencies 9,100 and 2,980 Mc./s. began at 1322 U.T. The onset of the main steep rise occurred at 1324. At frequencies 545 and 200 Mc./s. the onset occurred definitely later, at 1326·5 and 1327·5, respectively. The intensity curve of the unusually strong outburst at 2,980 Mc./s. is reproduced in Fig. 2.

The polarization behaviour at 200 Mc./s. was as follows. During the first 3·5 min., from 1327·5 to 1331, the Nera polarimeter indicated very irregular polarization, fluctuating between right-handed and left-handed. The degree of polarization is unknown, because the total radiation recorder was at first largely off-scale; but it was certainly very small. The irregular polarization behaviour suddenly came to an end at 1331. Perhaps this marks the end of a 'first part' event, which may have been a type II

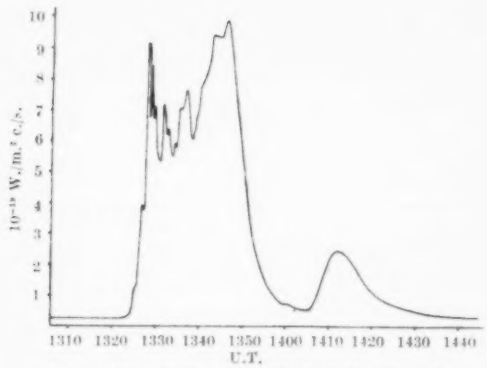

Fig. 2. The outburst at 2,980 Mc./s. on November 12

outburst. From 1331 on, the radiation showed about 35 per cent uniformly right-hand polarization. This sense of polarization, which was prevalent throughout the period under discussion, is opposite to the left-handed sense normally associated with sources on the northern hemisphere during the present sunspot cycle.

Cosmic Rays

Observations of the low-energy part of the cosmic radiation are obtained at Nera with a standard duplex neutron monitor. At about 1400 U.T. on November 12 the intensity increased, to reach a first maximum of 13 per cent above the initial level at about 1500. A second increase started at about 1745, to reach a maximum of 56 per cent at about 1930 (Fig. 3). This rise was approximately coincident with a strong increase of geomagnetic activity at

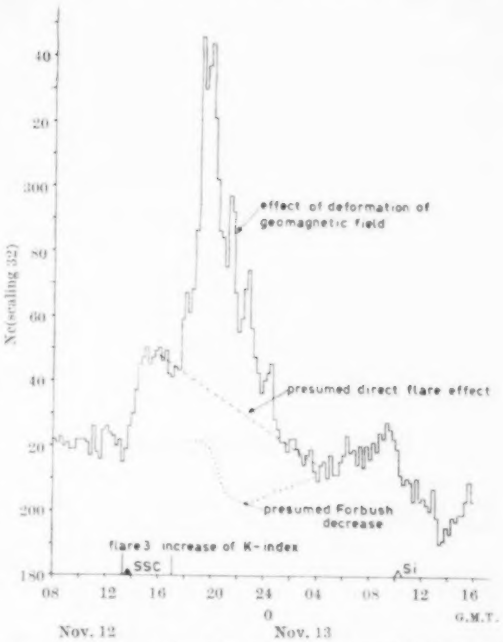

Fig. 3. Cosmic-ray flare effect observed with standard duplex neutron monitor at Nera. The diagram represents 15-min. values, corrected for air pressure

about 1710, following the sudden storm commencement (SSC) at 1348.

The increase of cosmic-ray intensity at about 1745 is most probably due to a lowering of the Störmer cut-off energy valid for the geomagnetic latitude of Nera (53·9°). This lowering of cut-off energy is obviously a consequence of the deformation of the Earth's magnetic field during the violent stage of the geomagnetic storm. Increases in cosmic rays at geomagnetic latitudes lower than normal have been recorded several times during geomagnetic storms with balloon equipment[1]. The event of November 12 represents the first instance in which it has been possible to establish this effect by means of ground observations.

At lower latitudes a Forbush decrease was observed towards 22h. U.T. This decrease is masked in our observations by the cosmic-ray flare effect, except perhaps for the later stage of its recovery (see Fig. 3).

The cosmic-ray increase on November 15 amounted to 15 per cent. The effect had a very regular course and lasted 10 hr.

Earth Current Observations

The cosmic-ray flares of November 12 and 15 were also distinctive in producing exceptionally large solar-flare effects ('crochets') in earth potential measurements at the equatorial stations Paramaribo and Hollandia, respectively.

In the period under discussion, there were two sudden storm commencements. In Table 1 we indicate the flares that can be held responsible for these SSC's. The two flares of November 12 and 15 did not cause an SSC proper, probably because their contribution to geomagnetic activity was superimposed upon already existing disturbed conditions. However, their influence can be traced tentatively in the following way: (1) on November 13 at 1022, 21 hr. after the November 12 flare, a sudden impulse of world-wide character occurred, followed by strongly reinforced geomagnetic activity lasting for several hours; (2) on November 15 at 2202, almost 20 hr. after the November 15 flare, there occurred a world-wide reinforcement of geomagnetic activity, lasting for several hours.

We note the remarkable parallelism in the sequences of events which results from these two suggested connexions:

Flare	Geomagnetic event	Interval (hr.)
November 11, 0311	SSC, November 12, 1348	34·6
November 12, 1322	*s.i.* + increased storminess, November 13, 1022	21·0
November 14, 0336	SSC, November 15, 1303	33·5
November 15, 0217	Increase of storminess, November 15, 2202	19·8

These two sequences were separated by a period of relative quietness setting in on November 14 at about 0200 U.T.

[1] Winckler, J. R., *J. Geophys. Res.*, **65**, 1331 (1960).

THE EYE, THE BRAIN AND LAND'S TWO-COLOUR PROJECTIONS

By Dr. W. A. H. RUSHTON, F.R.S.
Physiological Laboratory, Cambridge

GREAT interest has arisen from the spectacular demonstrations of Land[1] wherein the superposed projections of two black-white pictures, one through a red glass, can result in a scene filled with varied colours, including good greens and even some blues. Many have said that this disproves the 'classical' view that vision is trichromatic, since Land's colours are obtained with only two projection lights and are named as belonging to almost every region of the spectrum. A few have said (for example, the scholarly comment of Judd[2]) that the results show little that should surprise anyone properly acquainted with previous work. However this may be, it is a fact that in ordinary circumstances red mixed with white is called 'pink' (desaturated red); but in Land's conditions it may be called 'green'. What has happened to the eye or the brain?

Additivity in Monocular Matches

Colour-naming is notoriously unquantitative and hard to analyse, so here we rely on colour matching. The Land projection equipment was built by Dr. A. Karp[3] in the Cambridge University Engineering Laboratories, and lent to me by courtesy of Prof. Hawthorne. Red and white projection lights were superposed, each variable in intensity by partly crossed 'Polaroids'. The picture was a square subdivided into 25 small squares each uniform but differing in the red/white ratio from its neighbours in haphazard fashion. Each small square subtended 1° at the eye and the appearance gave a patchwork in many colours from red to bluish.

Interposed between the observer and the picture was a small white card about one-third the area of a small square. It did not receive any light from the projectors, but was illuminated by a variable mixture of monochromatic lights, red (650 mμ), green (530 mμ) and blue (460 mμ), from a Stiles double monochromator[4], the energies of each component *R*, *G*, *B* being measured by interposing an E.M.I. photomultiplier tube.

Experiment 1. By suitably adjusting the *RGB* mixture, the card could be made indistinguishable from the small square on which it appeared to lie; for example, seen against a green square the card could be made an identical green. The red projector light was then extinguished, so the card was seen against a grey square surrounded by other greys. The card now appeared bright *pink* though the spectral lights on it had remained untouched. This was to be expected, for initially the card matched the square, so when the red component was removed from the square it should be seen in excess on the card. This expectation proves exact, for if the *RGB* energies on the card are measured when matched with the square illuminated by: (*a*) the white projection only; (*b*) the red only; (*c*) both together, it is found for each of *R*, *G* and *B* that the energies in (*c*) are the sum of those in (*a*) and (*b*).

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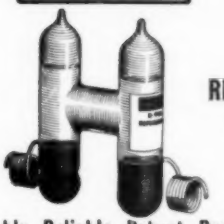

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It is a well-known feature of the Land picture that its general appearance is little affected by the relative intensity of the two projection lights. Though the 'warmth' of the picture is altered, the red square and the green square are still so named after the ratio of the projection lights has been greatly changed. What happens in these circumstances to the *RGB* proportions on the matched comparison card?

Experiment 2. The card was placed in front of a green square and matched, the red and the white energies falling on the *square* being measured by interposition of a photomultiplier tube. Now the projection image was shifted across the screen so that, for example, a red square lay behind the card. The two projection intensities were altered so that the energies received on this (still red) square were the same as they had been on the former green one. The unchanged light falling on the interposed card matched perfectly this new square, but now it looked red, not green. Every square with red-white energies adjusted to these fixed values was matched by the fixed card which assumed the colour of each square in turn when viewed in that particular location in the picture.

Conclusion from Monocular Matches

The results are simple and 'classical', being in accord with the law which Grassmann[5] enunciated more than a century ago, namely, that two lights which appear identical in one situation appear so in all. The *RGB* mixture required to match any square is simply the sum of the energies required to match the white component and the red component falling separately on that square. The match is therefore dichromatic, and the projection of two lights, so far from exhibiting 'every colour', leaves enormously more colours unrepresented than those capable of being displayed. This may readily be seen by making a perfect *RGB* match for any Land projection and then altering any one of the *RGB* components to any extent. Every one of the colours so formed is neither produced nor producible by the Land projections employed whatever their ratio or intensity. If we believe that there are three cone pigments in the human eye, all the foregoing matching results may be shown to follow as an inescapable logical consequence.

A fine painting may evoke so realistic an appearance of depth that it is hard to believe that all we see is a flat sheet. There is a sense, then, in which we may say that three dimensions have been represented by only two, but the sense is artistic rather than scientific. It is in a similar sense that we may say that Land's art has evoked the three dimensions of colour.

Complexities in Binocular Matches

We have seen with monocular matches that when considerations are restricted to judgments of identity or non-identity, the relations are precisely of the kind that would be found if the eye were replaced by three photocells each with different spectral sensitivity. So much is entirely expected; what is surprising is our sensation, for example, that a fixed light looks now red, now green. What is bewitched by Land's magic lantern? Is it the eye—or is it the brain? Perhaps when a red light appears green the eye is still sending the normal 'red signal' up the optic nerve, but the brain, confused by messages from the retinal surround, decodes the signal incorrectly. This suggestion can be shown to be wrong. For if it were right a similar normal 'red signal' coming to the brain from the other eye would also be decoded incorrectly in precisely the same way, and hence look the same. (For simplicity of treatment the 'brain' is here considered as a single decoding device operating equally on the messages from each optic nerve and delivering a decoded output which stands in one-to-one relation with visual sensation.)

Experiment 3. One may look with the left eye at the green square in the Land projection, and with the right eye down a tube observing nothing but a card illuminated by the *RGB* mixture from the monochromator. If the mixture on the card matches the green square by monocular superposition it is generally found not to match at all viewed binocularly; the square looks green, the card looks pink, so the left eye cannot be transmitting a normal red signal.

The signal which is being transmitted will be the same as that in the right eye when a binocular match has been established. But Land's colours in general cannot be matched by any spectral mixture seen in the other eye. The browns, olives and greys have too much black in them. This difficulty was overcome by surrounding the card presented to the right eye by a white background of about the colour and intensity of the white Land projection alone.

Experiment 4. These matches were not very easy to make but were reasonably repeatable, and the *RGB* mixture when later observed alone corresponded roughly with the remembered appearance of the particular square matched, so the green-appearing square was matched by a green part of the spectrum (blackened by contrast to the white surround). The particular spectral wave-length corresponding to the *RGB* mixture could be found from the colour triangle of Wright[6] whose primary wave-lengths we have adopted.

Experiment 2 was repeated but with binocular matches made against various squares, each adjusted to receive a fixed energy from the white and from the red projector. The results were quite different from those of Experiment 2, where the match was monocular. Each square now needed a different *RGB* mixture and the (darkened) spectral colour resulting corresponded fairly well to the coloured appearance of each square as seen in normal viewing.

When a binocular match has been established it is plausible (though not certain) that the signals in the two optic nerves are the same. Therefore the binocular match will measure that part of the 'Land effect' which is due to unusual encoding by the eye. It cannot give information about that part which is due to unusual decoding by the brain, since this will be the same for both nerves. That abnormal decoding may be involved, however, is seen from the following experiment.

Experiment 5. A narrow tube is pointed at the Land figure so that on looking through the tube all that is seen is part of one square. First the whole picture is viewed and that particular square noted; then on looking through the tube its colour is seen unaltered, nor is any change seen on continued observation.

Here is a paradox, for when this experiment is repeated with various squares, each adjusted to receive the same red and white projection energies as in Experiment 2, we have the extraordinary situation in which the eye looks through the tube at an isolated and identical red-white mixture and sees this as a colour which persists (though with dwindling conviction) with a hue which may vary greatly depending upon the past history. It will in fact be the colour

of the square as seen previously in the full picture. Though this colour persists—or rather is not seen to change so long as one looks down the tube at the unchanging square, it alters instantly on glancing at a new surround and back down the tube. This persistent memory and sudden change of judgment suggest activity of brain, not eye, and binocular comparison confirms it.

Experiment 6. A binocular match was made as in Experiment 4, and suddenly the surround to the small square was removed by interposition of the tube at the left eye. The binocular match was immediately upset and for restoration needed an *RGB* mixture close to the proportions for the monocular match, though the white surround to the comparison field made a perfect match unobtainable.

This experiment shows that when the surround field is abolished in the left eye the encoded message (as judged by the colour match in the right eye) changes at once to the normal 'pink message'. But it is not seen to change if viewed without binocular comparison. The decoding mechanism in the brain, therefore, either is insensitive to this change of message or it deliberately compensates for it. The first possibility is excluded by the fact that a much smaller alteration in nerve message produced by slightly changing the red/white ratio of the projection lights is easily detected.

We thus arrive at the surprising conclusion (though familiar to psychologists as an example of 'colour constancy') that when the same square is observed through the tube and in the open, the brain in some way recognizes the identity and in its decoding exactly compensates for the change in the message which it receives: and, indeed, when a green square is matched binocularly and then has its surround abolished, the sensation experienced is not that the square goes pink, but that the comparison card suddenly gets more green—at least if one's attention is fixed primarily upon the square. But I am trying to avoid speaking of my sensations!

Conclusions

This article reaches some over-simplified and rather obvious conclusions about the difficult subject of colour appearance.

(*a*) It is easier to analyse by colour matching than by colour naming.

(*b*) Monocular matches are simply the sum of the matches made with each component of projection alone. They follow Grassmann's law and the logic of three cone pigments.

(*c*) Colour appearance may depend on the surrounding field and its past history. These alter the encoding of nerve messages by the eye, and decoding by the brain.

(*d*) The extent of the former may be measured by binocular matches, the extent of the latter by memory matches.

(*e*) The eye–brain model postulated is crude, but it reveals some of the complexity which underlies the sensation of colour.

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[2] Judd, D. B., *J. Opt. Soc. Amer.*, **50**, 254 (1960).
[3] Karp, A., *Nature*, **154**, 710 (1959).
[4] Stiles, W. S., Thomas Young Oration. *Phys. Soc. Year Book*, **44** (1955).
[5] Grassmann, H., *Ann. Phys.* (Lpz.), **89**, 69 (1853).
[6] Wright, W. D., *Researches on Normal and Defective Colour Vision* (Henry Kimpton, London, 1946).

OBITUARIES

Prof. P. G. H. Boswell, O.B.E., F.R.S.

Few geologists have accomplished more in the face of chronic ill-health than P. G. H. Boswell, emeritus professor of geology of the Imperial College of Science and Technology, London, who died on December 22, 1960, at Ruthin, North Wales, at the age of seventy-four. Not only did he contribute close on 150 publications, including several memoirs and books, but also he was for long vigorously engaged in teaching and administration at the Universities of Liverpool and London, in the conduct of learned societies, and in proffering geological advice to various industrial and public undertakings.

Born at Woodbridge, Suffolk, in 1886, he developed during adolescence such an absorbing interest in the geology of his native county that in 1912 he abandoned teaching in an elementary school so as to concentrate on geology by studying under W. W. Watts at the Imperial College. While there he continued his researches on the Pliocene–Pleistocene succession in East Anglia and helped to correlate Early human phases with those of the Glacial Period, besides devoting much attention to the Chalk and to an assessment of the magnitude of the Eocene unconformity in the London Basin.

It was while investigating the Tertiary rocks that his thoughts turned to the possibility of using their detrital mineral assemblages for correlating particular horizons. This led him to specialize in the quantitative and qualitative aspects of sedimentary petrology which were to prove so helpful in deciphering the palaeogeography, tectonics and climatic conditions of past epochs, and so valuable in connexion with the search for glass-making, moulding and refractory sands during and after the First World War. Shortly after his appointment to the chair of geology at Liverpool in 1917, Boswell started his protracted researches, lasting more than twenty-five years, into the stratigraphy and tectonics of the Silurian rocks of the Denbighshire Moors. Even though some of his structural interpretations have been assailed, there is no doubt that most of his observations, gathered together in a volume on the *Middle Silurian Rocks of North Wales* (1949), will stand the test of time. Always actively interested in the applications of geology to civil engineering, his advice during the planning and construction of the Mersey road tunnel contributed in no small measure to the success of that major project.

In 1930 he was invited to succeed Watts as professor of geology at the Imperial College, but his tenure of the chair was comparatively brief, for he was compelled to resign eight years later because of ill-health. Nevertheless, he continued his work in North Wales and his consulting practice until 1953; thereafter, though gravely incapacitated, he still wrote a number of papers on thixotropy, greywackes and allied subjects, ending with a treatise on muddy sediments, to be published posthumously.

Boswell had been president of the Geological Societies of Liverpool (1921–23) and of London

(1940–41), of the Prehistoric Society (1936), and was successively general secretary (1931–35) and general treasurer (1935–43) of the British Association, besides being president of Section C (Geology) in 1932. Other honours included the Bigsby Medal of the Geological Society of London (1928), election to the Royal Society (1931), and honorary membership of many scientific societies at home and abroad; he was made O.B.E. in 1918. He will be remembered with affection and esteem by all his former colleagues and by generations of students, not least by those he inspired at Liverpool during the hey-day of his career.

DAVID WILLIAMS

Prof. E. T. Bell

E. T. BELL, who died in 1960, was born at Aberdeen in 1883. His schooldays were spent in Great Britain, but he attended university in the United States, where he spent the whole of his adult life. He occupied a number of university posts, culminating in his tenure of the chair of mathematics at the California Institute of Technology, Pasadena, 1927–53.

As a schoolboy, Bell came under a mathematical teacher of rare distinction, E. M. Langley, of Bedford, and on Langley's death wrote with warm appreciation of being shown something of the mode and content of modern mathematics by an inspiring teacher, and in particular of being introduced at school to the theory of numbers and to elliptic functions. His research work was mainly in those fields, and he made significant contributions to the classical theory of numbers, the field of rational arithmetic and of Diophantine analysis.

Bell's name, however, was well known outside the restricted circle of professional mathematicians, by the series of books, from about 1930 onwards, in which he endeavoured, with substantial success, to explain modern mathematics to the intelligent layman. Of these books, three deserve special mention. In *Mathematics, Queen and Servant of Science* (1952), a conflation of two earlier volumes, he described the dual nature of mathematics, its remoteness from prevalent crude materialism and its extraordinary knack of becoming vitally relevant to material concerns. If there are two cultures, mathematics, belonging to both, is the essential bridge between them. *Men of Mathematics* (1937) relates the outstanding mathematical discoveries of the ages to the men who made them; sufficient personal detail is given to allow the reader to see mathematicians as human beings, but emphasis throughout is on their contributions to mathematics. Something of the same theme runs through *The Development of Mathematics* (1940), which is not an encyclopædic history of the subject, but a narrative of carefully chosen main trends, themselves presented through typical major episodes; it is a graphic map of the main roads, and omission of byways and dead ends is deliberate and justifiable. Even so, the amount of information and opinion packed into 550 pages is extraordinary.

Bell's facts are almost always sound, his style is clear and exuberant, his opinions, whether we agree with them or not, are expressed forcefully, often with humour and a little gentle malice. He was no uncritical hero-worshipper, being as quick to mark the opportunity lost as the ground gained, so that from his books we get a vision of mathematics as a high activity of the questing human mind, often fallible, but always pressing on in the never-ending search for mathematical truth.

T. A. A. BROADBENT

NEWS and VIEWS

Royal Geographical Society: Medals and Awards

H.M. THE QUEEN has approved the award of the Royal Medals for 1961 of the Royal Geographical Society as follows. *Patron's Medal:* Mikhail M. Somov, deputy director, Arctic and Antarctic Research Institute, Leningrad, for polar exploration and research; *Founder's Medal:* John Bartholomew, editor, *The Times Atlas of the World*, for contributions to cartography.

The Council of the Royal Geographical Society has made the following awards. *Victoria Medal:* Prof. W. William-Olsson, Stockholm School of Economics, for contributions to economic geography; *Murchison Grant:* Prof. K. M. Buchanan, University College, Wellington, New Zealand, for contributions to economic geography; *Back Grant:* Eric H. Brown, University College, London, for geomorphological research; *Cuthbert Peek Grant:* Martin W. Holdgate, Scott Polar Research Institute, Cambridge, and leader of the Royal Society's Expedition to southern Chile; *Gill Memorial:* Cuchlaine A. M. King, University of Nottingham, for glaciological and coastal research; *Mrs. Patrick Ness Award:* R. M. L. Mason and A. R. Hanbury-Tenison, for their trans-continental exploratory journey in South America.

Statistics at Birkbeck College, London: Prof. D. R. Cox

THE establishment of a chair in statistics at Birkbeck College, University of London, marks the fulfilment of a scheme the authorities have had in mind for some few years of establishing statistics at the College. Birkbeck College is a college of the University of London reserved for students who are in full-time occupation, so that the majority of the students attend only in the evening. In the past, the object of the College was to provide a university education for students who, for financial or other reasons, were unable to secure this in the normal way; but the development of university education in Britain has introduced many new elements. It is now much easier for a student to secure full-time education; on the other hand, there is now a need for many more men with qualifications in two allied subjects, and the College is finding that more and more of its students are fitting into this class. In particular, there are many who have taken degrees in mathematics who wish to obtain a qualification in statistics, and in developing this new department, the College has the needs of these students particularly before it. The department will provide courses for postgraduate and undergraduate students.

Dr. D. R. Cox, reader in statistics in the College, has been appointed to the new chair. His interests are the scientific and technological applications of statistics and probability, and the theory of statistics. His published work includes a book on the *Planning of Experiments* and he is joint author of a book on the theory of queues to be published shortly. His present research interests include prediction theory, various applications of the theory of probability in operational research, and the design and statistical analysis of experiments.

Division of Pure Physics, National Research Council of Canada: Dr. D. C. Rose, O.B.E.

Dr. D. C. Rose has been appointed director of the Division of Pure Physics, National Research Council of Canada. Dr. Rose was born in Prescott, Ontario, in 1901, and gained his B.Sc. degree in 1923 and his M.Sc. degree in 1924 from Queen's University. He was awarded an 1851 Scholarship for study, under Rutherford, at Cambridge, where he obtained his Ph.D. degree in 1927. After continuing his work at the Cavendish Laboratory until 1928, he spent 1928–29 at the H. H. Wills Physical Laboratory, Bristol, and 1929–30 as a lecturer at Queen's University. In 1930 he joined the Division of Physics of the National Research Council of Canada. During the Second World War, Dr. Rose was seconded to the Department of National Defence, first as scientific adviser to the Chief of the General Staff, during 1943–45, and later, during 1945–47, as chief superintendent of the Canadian Armament Research and Development Establishment at Valcartier. Returning from war-time duties to the National Research Council, he established a laboratory in cosmic-ray physics, which he still heads. For his contributions to the war effort, Dr. Rose was made O.B.E. Dr. Rose was elected a Fellow of the Royal Society of Canada in 1936; he has served the Society for several years as secretary of Section III. He is a past president of the Canadian Association of Physicists, a member of the American Physical Society and a member of the Engineering Institute of Canada.

Building Contracts for Universities

In his report to the University Grants Committee reviewing the methods used by universities of contracting and of recording and controlling expenditure, Sir Arthur Rucker has some fourteen conclusions relating to the recommendations of the Gater Committee. The appointment of a small project sub-committee for each major building project is generally desirable and now usual, and this sub-committee should have in mind both the user's need and the needs of economy. There is occasionally difficulty in finding suitable persons with business and financial experience from outside a university to serve on the council and committees of the university, but every effort should be made to do so. Universities should keep their needs for staff under review to ensure that they and their committees have the advice and assistance they require to maintain proper control in their expanded building programme. No university should include in the list of firms invited to tender for a building contract any firm to which, if it were the successful competitor, the university would not desire to award the contract. Undue economy in capital costs at the expense of maintenance costs would be regrettable, but in a well-designed building it should be possible, within a reasonable over-all cost, to use materials and methods that will avoid excessive future maintenance costs.

It is important that all possible means should be sought both to make the maximum use of costly university buildings and to avoid planning new buildings on too low a standard of student use. Economy will always best be served by avoiding a break in the continuity of construction, and this should normally be possible in the present enlarged building programmes. The control exercised by universities and their committees and by the University Grants Committee over variations in plan after tenders have been invited is firm, and it is essential it should remain so. The normal practice of universities is, and should continue to be, to invite competitive tenders on a fixed price basis; in suitable cases negotiated contracts may be advantageous. Methods of letting sub-contracts have varied, but none of the methods used appears to have caused difficulty. The selection of sub-contractors before the letting of the main contract is, however, desirable. It is usually necessary to specify the date by which a contract is to be completed in the tender form, but the date should not be a matter for competition. The present practice of providing a sum for contingencies not exceeding 3 per cent appears to be generally satisfactory to universities, and is satisfactory so long as it is used for true contingencies and not for changes in plan. Architects should be required by all universities to make regular written reports to the responsible committees at least once a month, and in all universities the responsible committee should be provided at regular intervals with figures showing the estimated final commitment on each major contract. The general features of the Rucker Report are discussed elsewhere in this issue of *Nature* (p. 427).

Student Wastage in Australia

According to a *Times* correspondent, Prof. R. Le Fèvre, professor and head of the School of Chemistry in the University of Sydney, has stated that that University failed 1,000 first-year students who sat for chemistry examinations in 1960. Prof. Le Fèvre said that if failures in other science subjects were included, the failure-rate would be about 50 per cent. There were too few lecturers and too many students. "We have a British university system imposed on an American schooling system. What we need is something like the American junior college system or the British sixth form which provides a suitable bridge between high school and university." Prof. Le Fèvre said that some students did not know how to work and some just wanted to have a good time. The only solution appeared to be the introduction of some kind of pre-selection system.

There seems to be little doubt that, so far as science, in any event, is concerned, the Australian system needs serious overhauling. Far too much time, money and space are wasted in the training of first-year students. This is, of course, to the detriment of standards within the university itself; but even worse is the fact that such student failures have apparently wasted one year of the most formative phase in their lives.

International Laws on Nuclear Incidents

The Convention on Third Party Liability in the Field of Nuclear Energy, of July 29, 1960, was signed at Paris by the Governments of the West German Federal Republic, Austria, Belgium, Den-

mark, Spain, France, Greece, Italy, Luxembourg, Norway, the Netherlands, Portugal, the United Kingdom, Sweden, Switzerland and Turkey. The text of the Convention, which has now been published by the Organization for European Economic Co-operation, contains 24 articles (Pp. 67. Paris: O.E.E.C., European Nuclear Energy Agency, 1960). Its scope is limited to risks for which common law rules and practice are unsuitable, and it does not apply to nuclear incidents occurring in the territory of non-contracting States or to damage suffered in such territory. Its special regime applies only to nuclear incidents occurring at or in connexion with certain nuclear installations or in the transport of nuclear substances as defined. Risks which arise in respect of radioisotopes used for any industrial, commercial, agricultural, medical or scientific purpose are excluded, once the radioisotopes are applied for those purposes, as such risks are not exceptional: nuclear propulsion and nuclear fusion are also excluded, for different reasons. All liability for installations is channelled on to the operator of the nuclear installation where the incident occurs, while liability for incidents in transport falls either on the carrier or on the operator of the nuclear installation concerned. There are detailed provisions determining the kind of damage which will be compensated, and maximum liability in respect of any single incident has been fixed at 15 million European Monetary Agreement units of account, and rights of compensation are extinguished ten years from the date of an incident if no action has been brought before a competent court.

Detection and Identification of Underground Explosions

In connexion with the work of the conference on nuclear test control at Geneva, the Government recently announced its intention to carry out a programme of seismic research bearing on the detection and identification of underground nuclear explosions. This programme is now being planned in detail by the U.K. Atomic Energy Authority and suitable areas for the siting of seismic measuring instruments are being investigated. The research programme will involve the firing of conventional explosive charges, but no nuclear explosives will be used. Some of the firings will probably take place in disused mines and quarries: others may take the form of charges dropped at selected points in the Channel from naval vessels. An operational centre for seismic work is being established at a converted country house a few miles from Aldermaston.

The Field Studies Council

A wide range of courses dealing with many topics has been arranged by the Field Studies Council for 1961. At certain periods, normally March–Whitsun, there is great pressure on accommodation at the Centres and priority is given to members.

The Easter courses for schools are now designed for second- and third-year sixth-form pupils only. For pupils in secondary modern schools, a number of countryside courses have been arranged. The programmes again include a choice of courses specially designed for teachers in primary, secondary modern and grammar schools. At all times, even when courses have been arranged, places are kept for artists, amateur naturalists and other individuals or groups who wish to organize their own programme or to pursue studies independently, or in a less formal way than is suggested by the word 'course'. The Council has at its disposal a small bursary fund which is available to reduce the fee charged in individual cases of merit where grant-aid is needed but is not obtainable. Among the more unusual courses is that at Dale Fort for teachers dealing with marine biology and oceanography as well as "Man in Pembrokeshire", a course in historical geography. At Flatford Mill a course is to be run for amateur entomologists introducing them to field techniques in insect ecology. Juniper Hall has a course on slugs and snails, while Malham Tarn has a special course on karstic landforms as well as one on spider ecology. Students of geomorphology will find a special course at Preston Montford, while Slapton Ley provides an introduction to field archæology. Details of these, as well as the more routine, courses may be obtained from the Publicity Secretary, Field Studies Council, Ravensmead, Keston, Kent.

Biology, Psychology and Belief

The fourteenth lecture in memory of Sir Arthur Eddington was delivered in Cambridge on November 3 by Dr. W. H. Thorpe. Dealing with the relationships between the biological sciences and religious belief, Thorpe's lecture takes a rightful place among the more outstanding of its predecessors. To this lecture Thorpe has brought an honesty of purpose which should be of considerable help to biologists confronted with difficulties in reaching some general system of faith. There is also a clarity of thinking which is concerned never to confuse but to paint a world of the spirit as revealed to Thorpe. That man is a biological, as well as a spiritual, organism is well brought out, as is the conviction that no system of faith or belief has any ultimate prospect of securing the loyal and lasting adherence of educated men in the twentieth and later centuries unless it is firmly rooted in biological fact. The lecture has now been published as a booklet and should appeal to readers of all disciplines concerned with the nature of spiritual belief (Pp. 60. Cambridge: At the University Press, 1960. 4*s*. 6*d*.).

Rock Shelters of the Lower Murray River

A recent issue of the *Proceedings of the Royal Society of Victoria* contains an interesting account of an excavation undertaken at Fromm's Landing on the Lower Murray River under the leadership of D. J. Mulvaney, of the University of Melbourne (New Series, 72. Pt. 2. Victoria: The Royal Society, 1960). A rock-shelter, facing east and well suited for habitation, was explored and no less than ten different levels determined. Not enough attention has been paid by prehistorians to recent work in Australia. Maybe the finds in various regions of Africa have too exclusively engrossed their attention. Australian Stone-Age sites have been dismissed as early native. The carbon-14 method of dating has many pitfalls and cannot always be entirely relied on unless many samples from a culture-level (and not all from the same site) have been examined. But the chances of reasonable accuracy are increasing as workers in the field are learning what precautions must be taken in procuring samples, and in the laboratory new techniques are being developed. The carbon-14 results for the lower levels at Fromm's Landing suggest a date some 4,000 years ago and one which therefore falls well within most prehistorians' periods.

Fromm's Landing is not the only site on the Lower Murray which has been explored: there is the Devon Downs shelter, with which Fromm's Landing can be compared, and there are others. As is to be expected, there are differences in the finds, both implements and fauna, as one proceeds from the top layer to layer 10. But these differences do not appear to be startling. Actually the site is not prolific in artefacts, but adzes, 'pirri' points (small, somewhat thick-based arrow-head-like affairs), microliths of various kinds and bone objects have been collected, as well as the bones of various mammals, reptiles, birds and fish. Naturally, too, shells, both univalves and bivalves, occur. On the walls of the shelter there are some rough markings, but these are scarcely worthy of the designation 'art'. The article is illustrated and the numbers under each illustration of a tool refer to accounts of them given in the text. There are, however, several such accounts referring to numbers which do not appear among the illustrations. Has a page of illustrations by accident been left out? The author is to be congratulated on an excellent piece of work. Should some of these habitation sites in Australia really date back to several thousands of years ago, it is high time geologists there took the matter up and determined a sequence of climate changes for the various areas in the continent. It is scarcely conceivable that no perceptible changes have taken place over so long a period. The correlation of such a climate sequence with the study of the stone industries from the various levels would mean an important addition to knowledge.

Birds of the Philippine Islands

It is known that the size of an island may be an important factor in determining certain characteristics of its avifauna. Recently, A. L. Rand and D. S. Rabor have directed attention to "a surprising but apparently very real phenomenon in the Philippines", namely, that species commonly restricted to higher altitudes may live at lower ones on small islands (*Fieldiana*: Zoology, **35**, No. 7, 221. Chicago: Chicago Natural History Museum, 1960. 4 dollars). Thus the fruit pigeon *Ptilinopus merrilli* is a mountain bird on Luzon, but lives at sea-level on the adjacent small Polillo Island; and there are similar cases. The brush cuckoo *Cacomantis variolosus* is of special interest because it lives on the mountains of Zamboanga, a large island of which the lower levels are inhabited by the related *C. merulinus*; on Siquijor (90 square miles) only *C. variolosus* is found, living far below what is regarded as its normal range. This observation may be considered with the known fact that there are species of wide distribution in south-east Asia which live only on small islands, the nutmeg pigeon *Ducula bicolor* being an example of this in the Philippine archipelago. The speculation is made whether a restricted montane habitat surrounded by lowlands may not in some way be equated to a small insular habitat surrounded by sea.

New Species of *Chaetacis* from South America

While working on collections of spiders in the British Museum (Natural History), Arthur M. Chickering of Albion College, Albion, Michigan, found numerous examples of the genus *Chaetacis* from South America. Chickering separated out specimens which appear to represent five new species, thus bringing the total number of known species to twelve. Two of the new species, which he describes in the August issue of *Annals and Magazine of Natural History* (**2**, No. 20; 1959), are represented only by males which have not previously been described, although apparently Eugene Simon saw one when he established the genus in 1895. The types are to be deposited in the Department of Zoology, British Museum (Natural History).

Measurement of Molecular Weights

An easy-to-operate device for the accurate determination of molecular weights of unknown materials in solution has been developed by R. A. Pasternak and Leonard A. Cavanagh, and is described in the November–December issue of *Research for Industry* (**12**, No. 6; 1960). This efficient analytical tool is also valuable for research on interactions of compounds in solution. The key to the instrument is a thermostatically controlled chamber, the atmosphere of which is saturated with the vapour of a solvent. A probe composed of two bead thermistors is enclosed. Drops of the solvent and of the sample solution are applied to the beads through one of the six syringe assemblies of the unit. At any given temperature the vapour pressure of a solution is lower than that of the solvent. Therefore, the solution drop warms up (by condensation of minute amounts of the solvent) until pressure balance between the two drops is attained. The temperature rise, detected by the thermistor probe, is about proportional to the 'osmotic concentration' of the sample solution. When the instrument is calibrated with solutions of known concentration, it is then possible to calculate the molecular weight of the unknown solution. The new instrument, which was developed for Mechrolab, Mountain View, California, has great advantages over present molecular weight devices. Because of the syringe assembly, it does not have to be opened after each sample. Indeed, duplicate readings can be taken on fresh samples within 1–5 min. An accuracy of 1–2 per cent is claimed. Moreover, only very small amounts of the sample are required for testing.

Fiftieth Anniversary Meeting of the Biochemical Society

The fiftieth anniversary meeting of the Biochemical Society is to be held during March 27–29, and will be centred on University College, London. The meeting will include a symposium and a memorial lecture. The symposium is to be on "Structure and Synthesis of Macromolecules" (March 27–28), and will be opened by Prof. F. G. Young (Cambridge). Among the other speakers are: Prof. P. Doty (Harvard); Prof. J. N. Davidson (Glasgow); Prof. E. L. Hirst (Edinburgh); Prof. W. Z. Hassid (Berkeley); Dr. M. F. Perutz (Cambridge); Prof. E. L. Smith (Salt Lake City); Prof. J. Monod (Paris). The third Hopkins Memorial Lecture will be given by Sir Hans Krebs, and is entitled "The Physiological Role of Ketone Bodies" (March 28). The annual general meeting and anniversary dinner will take place on March 29. Further information can be obtained from the honorary secretary, Dr. W. J. Whelan, Lister Institute of Preventive Medicine, Chelsea Bridge Road, London, S.W.1.

City of Liverpool College of Technology

It is announced that the following are to become honorary associates of the College: Mr. F. W. Adams (secretary and registrar of the Pharmaceutical Society

of Great Britain); Sir Edward Bullard (Department of Geodesy and Geophysics, University of Cambridge); Mr. E. Le Q. Herbert (president of the Royal Institute of Chemistry); Sir Alan Tod (president of the Liverpool and District Scientific, Industrial and Research Library Advisory Council).

University News : McGill University

THE research groups and weather observatory which have been responsible for the meteorology carried out at McGill University have now been supplemented by a Department of Meteorology, consisting of Profs. J. S. Marshall and F. K. Hare, Associate and Assistant Profs. R. H. Douglas, W. Hitschfeld, S. Orvig and B. W. Boville. In the undergraduate curriculum, four continuation courses in meteorology are available to the general programme toward the B.Sc. degree. For the post-graduate programme leading to the M.Sc., the normal admission requirement is a bachelor's degree with honours in physics, and there is no prerequisite meteorology. Candidates proceeding from master's degree to Ph.D. will continue as in the past to be primarily the concern of the research groups, with the possibility of some helpful backing from the Department. Prof. Marshall retains his title and duties as Macdonald professor of physics, and Prof. Hare continues as professor of geography and chairman of that Department. Profs. Boville and Orvig are known for their work in the Arctic Meteorology Research Group, and Profs. Douglas and Hitschfeld in connexion with the Stormy Weather Group. Until the present session, Dr. Douglas and Mr. Boville have been at McGill as members of the Canadian Meteorological Service, to which they have made important contributions. By the end of the present session their formal connexion to the Service will have been severed, but there will be close and continuing co-operation between this first Canadian University Department of Meteorology and the Canadian Meteorological Service.

Sheffield

Two new lectureships have been announced: Mr. A. Usher is to be lecturer in forensic medicine; and Mr. H. Merskey, to be lecturer in psychiatry.

Swansea

DR. J. D. WESTON, senior lecturer in mathematics, King's College, Newcastle upon Tyne, has been appointed professor of pure mathematics, to succeed Prof. R. Wilson, who retires at the end of the present session.

A one-year course, leading to a College diploma in chemical engineering, will be instituted in the session 1961–62. It will be open to students holding an honours degree, or equivalent qualification, in a branch of physical science or engineering, and the content of the course will be adjusted according to the background of the individual student. It will consist of lectures, tutorials, laboratory and design work, extending over a full academic session. Applications should reach the Registrar, University College, Swansea, by June 30.

Announcements

SIR JOHN COCKCROFT, master-designate of Churchill College, Cambridge, and part-time member of the U.K. Atomic Energy Authority, has been awarded the 1961 Atoms for Peace Award, for his contribution towards the application of atomic energy to the production of electricity in the United Kingdom. The Award, established as a memorial to Henry Ford and his son Edsel, consists of a gold medal and 75,000 dollars.

PROF. EPHRAIM KATCHALSKI, head of the Biophysics Department, Weizmann Institute of Science, has been awarded the Rothschild Prize for Research for 1960, in recognition of his work on the structure of poly-amino-acids.

MR. S. N. MITRA, of the Research Department, All India Radio, New Delhi, has been awarded the 1960 prize of the Council of the Institution of Telecommunication Engineers of India for his paper, "Magneto-Ionic Triple Splitting over Delhi".

PROF. W. T. ASTBURY, professor of biomolecular structure in the University of Leeds, has been elected the fourth recipient of the T. Duckett Jones Memorial Award. This is a medical award of 6,500 dollars administered by the Helen Hay Whitney Foundation, and it will be presented to Prof. Astbury at Princeton, New Jersey, on October 7, 1961.

MR. E. LL. HARRY, at present regional controller of the East Midland Region of the Ministry of Agriculture, Fisheries and Food, is to succeed Mr. C. D. Ross as regional director of the National Agricultural Advisory Service, South Western Region, when the latter retires on March 9.

A SYMPOSIUM and instrument exhibition on "Automatic and Semi-Automatic Methods in Analysis and Control" will be held at the Medway College of Technology on March 16. Further information can be obtained from the course organizer, Dr. D. T. Burns, Department of Science, Medway College of Technology, Maidstone Road, Chatham, Kent.

THE Faraday Society is organizing a general discussion on "Radiation Effects in Inorganic Solids" by invitation at the Centre d'Études Nucléaires de Saclay, Gif-sur-Yvette (S.-et-O.), during April 11–12. Further information can be obtained from the Assistant Secretary, Faraday Society, 6 Gray's Inn Square, London, W.C.1.

AN intensive short course in elementary plasticity is being organized by the Imperial College of Science and Technology, in the Department of Mechanical Engineering, during April 10–14. Further information can be obtained from Dr. J. M. Alexander, Department of Mechanical Engineering, Imperial College of Science and Technology, Exhibition Road, London, S.W.7.

THE Faraday Society is holding an informal discussion on the "Mechanisms of the Gas-Phase Reactions of the Halogens and their Compounds" in the Chemistry Department, University College, Cardiff, on March 28. The programme will be divided into two sections: (*a*) oxidation processes; (*b*) reactions of elementary halogens. Further information can be obtained from Dr. J. H. Thomas, Chemistry Department, University College, Cathays Park, Cardiff.

ERRATUM. In *Nature* of January 28, p. 275, concerning recent changes in administration and organization of the Akers Research Laboratory, Imperial Chemical Industries, Ltd., it was erroneously stated that Dr. Chatt will continue in charge of the Organic Chemistry Department; Dr. Chatt is in charge of the Inorganic Chemistry Department.

NEW LABORATORY OF LONDON TRANSPORT

By A. T. WILFORD

Director of Research

A NEW laboratory situated on London Transport's Chiswick Works Estate was officially opened by Mr. A. B. B. Valentine, chairman of the London Transport Executive, on December 5. It will continue the function of providing a scientific service available to all departments of London Transport and will permit an expansion of these facilities, with particular reference to engineering problems. At the same time, the small laboratories concerned with essential day-to-day chemical control at the three generating stations are being retained.

The history of the Chiswick Laboratory goes back to more than forty years ago, when a small laboratory was established by the former London General Omnibus Co. at Farm Lane, Fulham, primarily for testing petrol and lubricating oils. It was transferred to Chiswick Works, then newly opened, in 1921. The scope of its activities, mainly in the chemical field, gradually extended, and improved accommodation was provided in 1931. By the time that the London Passenger Transport Board was formed in 1933 the laboratory was beginning to provide a service also for departments of the undertaking other than those concerned with road vehicles, and in 1949 it became officially recognized as London Transport's Central Laboratory. Immediately prior to its transfer to the new premises, the Laboratory was housed in portions of four scattered buildings and three temporary huts on the Chiswick Works Estate.

The new Laboratory premises (Fig. 1) comprise a steel-framed two-storey building with an adjacent single-story annex, the total floor area being 27,000 sq. ft. Metallurgical, physics and engineering activities are housed on the ground floor, the chemical sections and general administration being located on the first floor. The single-storey annex contains a shop for manufacturing special chemical mixtures, also a pilot plant shop. Its roof is linked by a bridge to the first floor of the main building and serves as a site for weather exposure testing of paints. (A second exposure testing station, where conditions are somewhat more adverse, is maintained on the roof of the Executive's Upton Park Garage.)

Except in the engineering laboratories and workshops, the services, which include gas, electricity,

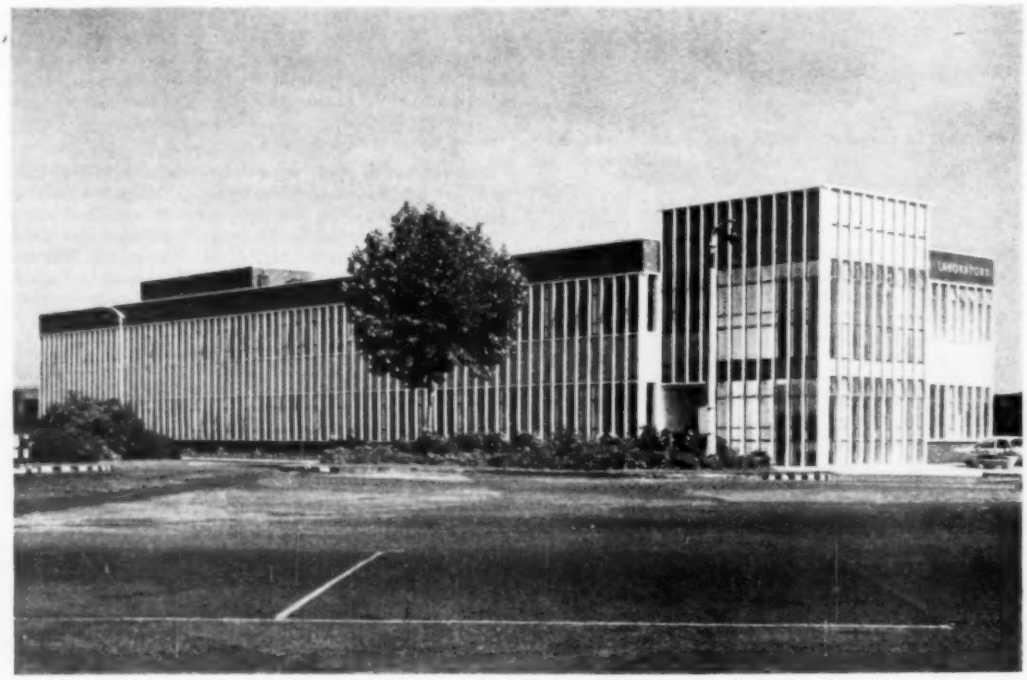

Fig. 1. New Laboratory of London Transport at Chiswick

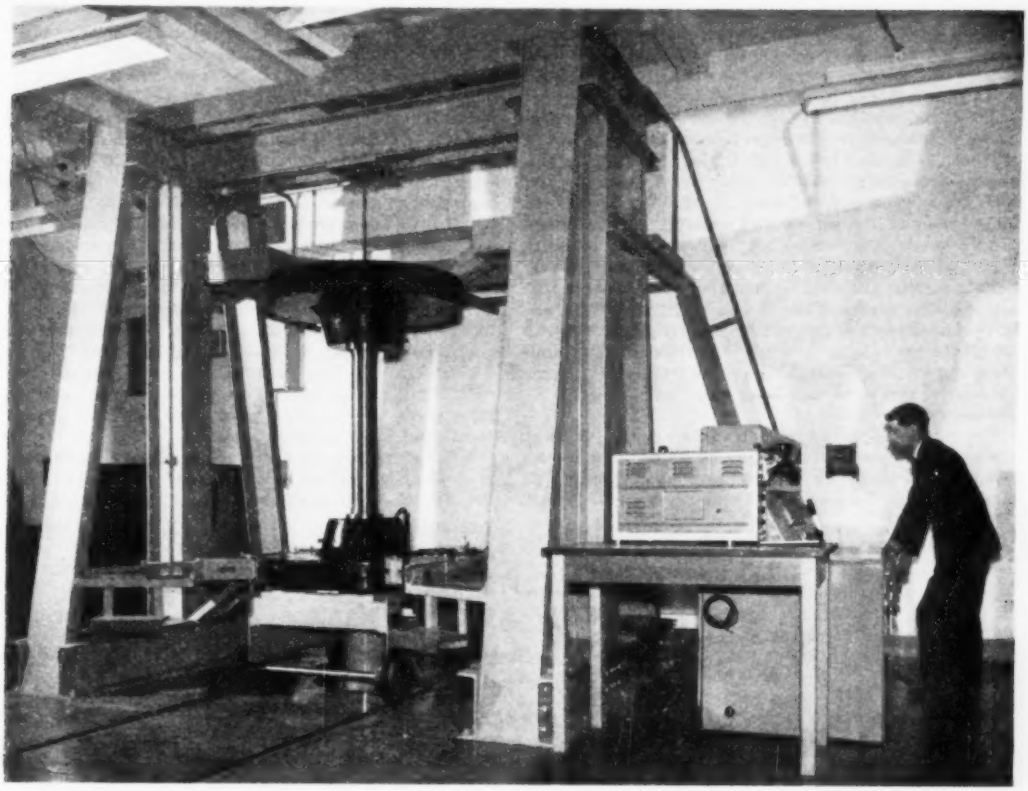

Fig. 2. Fatigue testing machine developed in the University of Nottingham

steam, hot water and pressurized cold water, are carried above removable ceiling panels, and the use of ceiling heating permits the most efficient use of laboratory floor space. Air extracted through fume cupboards, etc., is replaced by means of a plenum system which introduces air at a pre-adjusted temperature. Certain rooms are also provided with air-extraction systems.

The laboratory is concerned with chemical and physical control of supplies, technical control of works' processes and the investigation of many day-to-day problems which arise in the course of operation and maintenance of London Transport's services and where the specialized facilities available are likely to be of help. This work is essentially of a short-term character, but longer-term investigations are also undertaken, and special mention may be made of the pioneer work relating to the application of low-viscosity oil for lubrication of bus engines and improved lubricants for worm-driven axles; much work has also been done in connexion with lead–acid accumulators, in regard to fatigue failures of railway car axles, and on other problems relating to railway rolling stock and the permanent way.

The facilities for metallurgical work include a metals-chemistry laboratory, a laboratory for mechanical testing, a specially screened room with barium block lining for radiography, also rooms for macro- and micro-examination of metals and for technical photography. Equipment for heat treatment and welding tests is situated in the pilot plant shop. A well-equipped machine shop provides a service for all sections of the laboratory.

The physics laboratories include rooms for testing of batteries, photometric testing of electric lamps, non-destructive testing, high-voltage tests and construction and calibration of instruments. A cold chamber, 14 ft. × 9 ft. × 8 ft. high, is available for tests on equipment at temperatures down to about 0° F.; it can also be adapted for tests at elevated temperatures up to 120° F.

The chemical division of the Laboratory comprises three sections dealing respectively with fuels and lubricants, paints and protective processes and general chemistry, the latter being concerned with all chemical work other than that falling to the specialized sections. Separate 'general' and 'research' laboratories are provided for these various functions. In addition to its normal equipment, the fuels and lubricants section is equipped with an automatic oil oxidation apparatus, equipment for mechanical testing of lubricants and a small engine for determining the ignition quality of road-vehicle fuel. Equipment for testing paints includes a spray booth, stoving oven, an accelerated weathering machine and other apparatus for accelerated tests. There are also various instruments for physical testing, and a special room with direct access to the outdoor exposure station is provided for application tests, on which great emphasis is placed.

A textiles sub-section comprises a room for chemical and general examination of textiles and an

air-conditioned room for physical tests, the equipment of which includes a tensile testing machine with autographic recorder, a horizontal fabric strength tester and apparatus for abrasion tests, flex resistance and bursting strength.

The largest item of equipment at present installed in the laboratory is a fatigue testing machine which has been specifically designed to investigate the fatigue strength of railway car axles (Fig. 2). The machine has been developed at the University of Nottingham to determine the strength of specimens of axle steel when subjected to a rotation bending stress. There is a 'scale effect' of uncertain magnitude in fatigue and the machine is therefore designed to test specimens of typical axle sizes, namely, 6½ in. diameter. It is the intention initially to investigate the effects on fatigue strength of surface rolling and, later, the effect of shrink fits. The influence of composition of the steel and heat treatment will also be investigated.

The machine is of the resonant type, with a mechanical drive via a slipping clutch to permit starting and stopping. The specimen is about 5 ft. long × 6½ in. diameter with enlarged ends. Each end is secured in a heavy disk. The assembly of two heavy disks and the specimen as a spring has a natural frequency for transverse bending of the specimen just below 50 c./s. The assembly is freely suspended from the centre of one disk by a wire rope with the specimen vertical. The lower disk carries below it a rigid extension tube. If the lower end of this tube is made to move in a circular path at a speed corresponding to the natural frequency, the assembly is caused to vibrate and so give a rotating bending stress on the specimen. The stress is measured by resistance strain gauges, calibrated in position, and a number of protective devices are included so that the machine may be left running unattended. Two specimens have already been tested in the machine. One failed at a stress not much greater than the expected fatigue limit (2,910,000 cycles at 16 tons/in.²). The other failed at a higher stress (640,000 cycles at 20 tons/in.²). Both specimens were afterwards broken open by static bending to expose the fatigue-fractured surfaces.

The laboratory when up to strength will have a total staff of about eighty of all grades, one-third of whom will be graduates or otherwise professionally qualified.

TEXTILE RESEARCH INSTITUTE OF THE BOMBAY TEXTILE RESEARCH ASSOCIATION

By Dr. C. NANJUNDAYYA
Joint Director

THE cotton textile industry is one of the foremost organized industries in India and it has been playing its many-sided part making an increasingly valuable contribution to the country's economy and progress.

Although the need for organizing research on a co-operative basis was well recognized by the textile manufacturers of India long ago, the financial resources of the industry were not sufficiently encouraging to undertake any scheme in this behalf. It was only during and after the Second World War that impetus was given by the Government of India to promote and organize textile research. In order to implement this, the Government of India promulgated the Cotton Textiles Fund Ordinance in 1944, and constituted the Cotton Textiles Fund Committee for administering the funds raised by the levy of customs duty on yarn and cloth exported from India. This Committee, after due deliberations, decided to establish four textile research institutes, one in each of the four zones, into which the country was divided, and mills situated in Zone I, comprising the old Bombay State to the south of River Tapti, Madhya Pradesh and Hyderabad, were allotted to the jurisdiction of the Bombay Textile Research Association. It was further decided that, in the first instance, two research institutes, one at Bombay and another at Coimbatore, be established, ATIRA at Ahmedabad having already come into existence.

The Millowners' Association, Bombay, then took steps to formulate a scheme for establishing a Textile Research Institute at Bombay. Although the Bombay Textile Research Association was registered in 1954 under the Societies Registration Act, 1860, the preliminaries connected with the acquisition of a suitable plot of land, planning and other formalities connected therewith took some time. The actual construction of laboratory premises was commenced in 1958 on a 23-acre plot of land situated in very pleasant surroundings at Ghatkopar, a suburb of Bombay.

As the construction of the buildings and installation of the pilot plant and laboratory equipment were expected to take two or three years, at the instance of Dr. C. Nanjundayya, joint director, a building was taken on rent in 1958 and such technical work as could be carried out in the mills, namely, standards engineering, statistical quality control, technical liaison, physical and chemical testing, T.W.I., and dissemination of current technical literature, was commenced. As a result of the work done so far, the mills have begun to realize the benefits accruing to them from the Research Association.

The original scheme of the Textile Research Institute envisages a capital expenditure of about Rs. one crore (£750,000) and recurring expenditure of about Rs. 12 lakhs per annum (£90,000).

The scope of work of this Institute covers the entire field of textile research, comprising fundamental and applied research in the mechanical and chemical processing of cotton as well as man-made fibres, operational research, including statistical quality control and human relations, technical liaison for communication of results obtained in the laboratories to the mills and of mill problems to the Bombay Textile Research Association laboratories, an up-to-date technical library and dissemination of technical knowledge to mill technicians, and research in textile engineering.

The present built-up area of the buildings is about 100,000 sq. ft., which is approximately two-thirds of the area that is proposed to be built according to the original scheme.

It was on December 9 that the President of India, Dr. Rajendra Prasad, inaugurated the Textile Research Institute of the Bombay Textile Research Association. Dr. Rajendra Prasad was welcomed by Mr. Krishnaraj M. D. Thackersey, chairman of the Association; in doing so, he stressed the importance of research to the textile industry and said that it could profitably be carried out by co-operative organizations like the Bombay Textile Research Association, which has thirty-six large cotton mill companies as members. He further said that it was the desire and determination of the Research Association to see that the research and development work carried out in this Institute would materially help the textile industry not only to maintain its present level of prosperity but also to enable it to achieve further progress and prosperity.

Dr. Rajendra Prasad, in his opening address, appreciated the co-operative effort of the textile mills in the establishment and maintenance of the Research Institute for their common benefit, and said that it would supplement the general policy of the Government of India to encourage and undertake research in all fields. He was happy to know that the Association had the support of a large number of mills, and he had no doubt that the research done by the Research Institute would benefit the manufacturers, the consumers and the country at large.

Mr. Ramnath A. Podar, deputy-chairman, proposed a vote of thanks to the President, and Dr. C. Nanjundayya read a few of the large number of messages of good wishes received on the occasion from distinguished persons and institutions in India and abroad.

SECONDARY EDUCATION IN INDIA

IN 1952 the Government of India appointed a Commission (the Mudaliar Commission) to examine the prevailing system of secondary education in the country and to suggest measures for its reorganization and improvement. It is about six years since the report of the Commission and its recommendations have been before the public. These are now being considered for implementation by the State Governments under guidance and financial assistance from the centre (*Sci. and Culture*, 26, No. 4, 1960).

According to the new scheme for an eleven-years school course, education in secondary schools extends over 6–7 years. It is to be regarded as a complete unit by itself, and not merely a preparatory stage for the university and technical education.

This pattern of education has been framed generally after that of British countries, but it also includes some features of the American and Soviet systems.

The British pattern differs from that of the United States by providing for specialization at the secondary stage. In the United States, the secondary schools cater for a purely general, or academic, education as a preparatory step for admission to colleges in the university, and/or a vocational course as a preparation for earning a livelihood. The schools in the British countries provide both for those going on to universities and for those going directly into industries and commerce, or the public service.

The Commission has also borrowed some special features from the Soviet system of secondary education. This relates to the introduction of training for some crafts and fine arts in the curriculum so that instruction might be combined with some productive work.

The secondary school curriculum in India, now recommended, is a diversified one. A certain number of core subjects are, however, common to all students, irrespective of the diversified course of study taken by them. These are: (1) languages, (2) general science, (3) social studies, and (4) a craft. The diversified course of study consists of seven groups, namely (1) humanities, (2) sciences, (3) technical studies, (4) commercial subjects, (5) agricultural subjects, (6) fine arts, and (7) home sciences. Three subjects from any one of these groups are to be taken along with the core subjects.

A study of two languages has been recommended for the high and higher secondary stages. One of these must be the mother tongue or the regional language which forms the medium of instruction throughout the secondary stage. English and Hindi have been recommended for introduction in the earlier or lower secondary stage. English and Hindi have to be studied as compulsory languages by all, besides the regional language or the mother tongue.

The introduction of the higher secondary course has given rise to many serious problems, owing to the dearth of competent science teachers, the lack of proper laboratory facilities and equipment, and the shortage of suitable text-books in science subjects with precise descriptions of terms and terminologies for the regional languages.

A sudden increase in the school population at the end of the secondary stage, likely to result from the introduction of the eleven years school course, is another problem that has to be faced. Many of those coming out of the secondary schools will fail to find admittance to the university and professional colleges or the polytechnics; nor are they likely to be absorbed in sufficient numbers in government services or industries. The result will be an increase in unemployment. Though India is generally backward in education and has a literacy of only 17·5 per cent of the population as a whole, its relative position at the secondary level is abnormal in comparison with that of the most advanced countries of the world.

For every thousand students in the primary schools the number at the secondary and university stages for different countries are indicated in Table 1.

The structure of secondary education on India with a literacy of about 18 per cent of the population as a whole rests on an abnormally shrunken and narrow base. This represents instability, and is responsible for the comparatively poor standard of efficiency of the educational system. The remedy lies in the introduction of free and compulsory primary education as early as possible.

Secondary education for girls also represents a serious problem in India. The Mudaliar Commission is not in favour of making any distinction between education imparted to boys and girls in the secondary

Table 1

	No. of students per thousand		
	Primary stage	Secondary stage	University stage
India, 1956	60	23	1·8
China, 1955	87	7·4	0·5
Japan, 1956	144	90	6·8
West Germany, 1956	97	72	2·5
France, 1954	114	30	3·5
United Kingdom, 1954	108	49	1·6
U.S.S.R., 1958	125	38	10·5
United States, 1955	154	48	0·16
	No. of students		
	Secondary stage	University stage	
India, 1956	364	30	
China, 1955	84	5·6	
Japan, 1956	623	47	
West Germany, 1956	740	26	
France, 1954	264	31	
United Kingdom, 1954	453	15	
U.S.S.R., 1958	300	84	
United States, 1955	313	105	

schools, but recommends special facilities for the study of home science for the latter. Separate schools for girls have been considered preferable at the secondary stage, and definite conditions have been laid down for mixed co-educational schools to satisfy the special requirements of girl students and women teachers.

The Secondary Education Commission has considered defects in the present system of teaching and examinations, and has recommended certain changes. These include: reduction in the number of external or public examinations, change in the type of questions giving preference to the objective type of tests over the subjective or essay type, maintenance of a proper record of school work for every pupil, credit for the results of internal examinations and for school records in the final assessments by public examination, provision for only one public examination at the completion of the secondary course, and for compartmental examinations in case of failures in one or more subjects.

Even the organization of a single State-wide public examination at the completion of the secondary course each year is a formidable task as the total number of candidates in any State in India may easily reach a very high figure.

THE BRITISH COUNCIL

THE feature article accompanying the general survey of the year in the British Council's annual report 1959–60 deals with the printed word*. In doing so it gives a most readable account of the work of the Council's libraries and the way in which they foster the demand for British books and periodicals abroad. It includes details of the Council's own publications, and the information work, book exhibitions and book reviews which are incidental or ancillary to these activities. A brief summary of the action taken by the Government to promote exports of British books and periodicals is included. Of some 7,000 periodicals published in the United Kingdom, the Council uses, with yearbooks, some 1,750 in its work abroad and maintains more than 32,000 subscriptions not only for its own libraries but also for presentations, on local advice, to a wide range of schools and colleges, research stations and societies.

The general survey of the year notes that the Council is undertaking the general reception, accommodation, finance and welfare of scholars coming to the United Kingdom under the Commonwealth Scholarship and Fellowship Plan, as well as a corresponding responsibility for teachers from the Commonwealth coming for courses at teachers' training colleges. It has also been asked to help with the recruitment of teachers for schools in Commonwealth countries and with recruitment to university posts. Among developments overseas during the year, those in India and Pakistan are particularly stressed; by the end of 1960–61 the Council will have libraries in eight towns in Pakistan, six of them being university towns, while the tour by a team of eminent representatives of science and medicine in Cairo and the United Arab Republic is likely to increase the exchange of academic and professional visits between the United Kingdom and the Republic. In February 1960 the Council resumed work in Cairo. The programme of exchanges in the educational, cultural and scientific fields drawn up in March 1959 in Moscow with the U.S.S.R. was for the most part carried out, and for the first time British postgraduate students have studied for a full academic year in the Universities of Moscow and Leningrad while Soviet students have studied in British universities.

Between July 1957 and March 1960 the Council directly recruited 253 teachers of English and other subjects in English for overseas, and awarded 280 scholarships for training teachers for overseas in the United Kingdom. The continuing need for this work is again stressed in the report, and summer schools for teachers of English arranged during the year in the United Kingdom were attended by more than 700 teachers from overseas, while summer schools arranged overseas were attended by some 2,000 teachers. Overseas visitors under the auspices of the Council number 6,040, of whom 1,231 were from the Commonwealth and 381 from the Colonies; of these 1,052 were in medicine, 1,359 in science and technology, 1,125 in social science and 1,589 in education. A higher proportion is now coming from the Indian sub-continent and the Far East, and a smaller proportion from Europe. The programme of study tours continues to expand, and, of the 65 such tours arranged during the year, 15 were in science and technology. Stress is also laid on the value of the many specialist tours and advising visits overseas by leading figures in many professions which the Council arranges, and in regard to science the report refers to the continued financing of the exchange of senior scientists and research workers between the Royal Society and the U.S.S.R. Academy of Sciences, while the Royal Society was also enabled to invite a delegation from the Roumanian Academy of Sciences to visit Britain. The Council's current policy on books and periodicals places greater emphasis on scientific, technical and medical text-books.

* The British Council. Annual Report, 1959–1960. Pp. vi+110+12 plates. (London: British Council, 1960).

The total number of overseas students in the United Kingdom is estimated at about 47,000, and during the year the Council met on arrival 8,137 students as well as 1,299 United Nations' Fellows, Colombo Plan trainees, etc., who were assisted to find accommodation. Permanent accommodation in lodgings was found for 3,417 students, and for 405 in Council residences, and temporary accommodation for 5,005 while on study visits, etc., apart from transit or temporary accommodation in lodgings or Council residences for many more. Some 9,878 students enrolled as members of Council Centres during 1959, 2,736 attended vacation courses of 7–15 days, 1,481 week-end courses, and 9,554 half-day or full-day study visits to factories, museums, etc.

A SCIENCE PLANNING BOARD

THE proposal that the Government should set up a Scientific and Technical Planning Board to give "better direction to our scientific effort" is one of the recommendations for immediate action by the Association of Scientific Workers in a policy statement, "Science and Education"*.

The statement declares that, "given an adequate structure there is no reason whatever to fear a shortage of suitable people for higher education in science and engineering and teaching. Considerable untapped resources exist". The number of women in British technical colleges is very small compared with men. This difference is by no means due to innate intelligence or leanings, but largely to social customs reflected in school policies exacerbated by the desperate shortage of science teachers in girls' schools.

The Association's statement lists five objectives: to make science a central subject throughout the school lives of all children; to expand considerably the provision of educational opportunities for children beyond the age of fifteen; to overcome the critical shortage of science and mathematics teachers; to achieve a larger annual output of scientists and engineers than the present Government's targets, as soon as possible; to raise considerably the annual output of technicians of all kinds.

The report states that the first and most fundamental need is to provide more science teachers in schools and in technical colleges, training colleges and universities—and the most acute need is in schools. The only permanent solution to a shortage is to raise the salaries of teachers. The Association believes that "the immediate critical shortage" could be alleviated by a government-led national programme of secondment or release of scientists and mathematicians from the Civil Service (including the defence departments), nationalized industries and universities to teach in schools while the 'bulge' passes through, and a national drive to bring more married women back into teaching.

Proposals are also made to have at least four, and preferably six, new university institutions before the end of the 1960's; to expand the work of the technical colleges; to improve conditions of service of technicians in higher educational establishments; to assist more students to train to be scientists; and to make the fullest possible use of trained scientists, technologists and technicians.

* Association of Scientific Workers. Science and Education: a Policy Statement by the Association of Scientific Workers. Pp. 16. (London: Association of Scientific Workers, 1960.) 1s.

TOBACCO SMOKE RESEARCH

THE Tobacco Manufacturers' Standing Committee has as a declared aim the assistance of research into questions concerned with the relationship between smoking and health. That this object is being fulfilled is evident from its report for the year ended May 31, 1960, which summarizes investigations carried out during the year under the auspices of the Committee or with its financial support, including research into factors affecting smoking habits, the biological activity of tobacco smoke, factors affecting the incidence of lung cancer and certain other diseases and physiological and psychological aspects of smoking*. In addition to supporting these activities, the Committee has also made financial grants to the Medical Research Council and to the Institute of Cancer Research, Royal Cancer Hospital, London, for research into causes of lung cancer and into tumour viruses.

Fractions of cigarette smoke condensate prepared in the laboratories of the Committee have been found by several workers to have carcinogenic or tumour-promoting properties, but as the report points out, these results, obtained by application of smoke fractions to animal tissues, are not necessarily reliable guides to the possible response of human lung tissue to tobacco smoke.

Some of the investigations supported by the Committee have been stimulated by the suggestion of Sir Ronald Fisher that smoking habits may be influenced by genetic factors. It has been found in one investigation that the smoking habits of identical twins are more alike than those of non-identical twins, and other work into the personality characteristics of different types of smokers appears to confirm the view that genotypic differences exist between smokers and non-smokers and between cigarette smokers and pipe smokers.

The Committee has also published the first Supplement to its third research paper, "The Constituents of Tobacco Smoke: an Annotated Bibliography" (which is edited by H. R. Bentley and E. G. N. Berry)†. This useful compilation provides a convenient list of references, arranged in sections corresponding to chemical classes, covering the literature which appeared during 1959, and will be an invaluable guide to research workers in this field.

W. CARRUTHERS

* Tobacco Manufacturers' Standing Committee. Report for the Year ended 31st May, 1960. Pp. 11. (London: Tobacco Manufacturers' Standing Committee, 1960.)

† Tobacco Manufacturers' Standing Committee. Research Papers, No. 3: The Constituents of Tobacco Smoke, an Annotated Bibliography. First Supplement. Edited by H. R. Bentley and E. G. N. Berry. Pp. 1+25. (London: Tobacco Manufacturers' Standing Committee, 1960.)

THE WOLFSON FOUNDATION

THE first report of the Wolfson Foundation, created in 1955, covers the first five years work of the Foundation*. So far, the Foundation has adopted as its principal aims the advancement of education and health in the United Kingdom and Commonwealth, with particular reference to scientific and technological education, building for higher education, youth activities, medical research and education, cancer research, and medical, surgical and nursing services not covered by the National Health Service. Up to July 1958 it was occupied by preliminary work, including the creation of the necessary administrative organization and a Board of Trustees of wide experience and enjoying general confidence. To November 30, 1960, grants totalling £3,311,110 had been made and grants totalling a further £237,500 were made in December 1960. These latter grants, which are listed on a separate sheet issued with the report, include £100,000 to St. Hilda's College, Oxford, for a residential block for 60 undergraduates, £52,000 in extension for three years of the £125,000 already granted to the National Playing Fields Association, and £5,000 to the Commonwealth Society for the Deaf for a rehabilitation centre in Eastern Nigeria.

Grants for education noted in the report include £250,000 for a new Commonwealth Hall of Residence for 400 men students at the University of London; £65,000 to endow the Wolfson chair of metallurgy at the University of Oxford; and £4,500 for a research fellowship in metallurgy there; £300,000 for a hall of residence for about 150 men students at the University of Glasgow; £70,000 for an assembly hall forming part of the main block of Churchill College, University of Cambridge; £150,000 for the establishment of the Institute of Criminology in the University of Cambridge; £75,000 for building and furnishing the library of St. Catharine's College, Oxford; £350,000 to the Imperial College of Science and Technology to build and equip laboratories for biochemistry and chemical microbiology and support teaching and research in these subjects; £210,000 to the Royal Society to endow a research professorship; £100,000 to New Hall, Cambridge, and £80,000 to St. Anne's College, Oxford. A grant of £2,000 to the Royal Institution is a contribution to the Institution's work in interpreting current scientific developments to the public.

Major grants in the field of health include £250,000 to the Westminster Hospital School of Nursing; £150,000 over 10 years to the British Empire Cancer Campaign in support of its researches; £150,000 to the Postgraduate Medical School, Hammersmith, for the Wolfson Institute containing lecture theatres, common rooms and other amenities for students and teaching staff; £184,000 for the Institute of Psychiatry associated with Maudsley Hospital, University of London; and £450,000 to the Royal College of Physicians for a new building containing a larger library, a main lecture theatre seating 300, a smaller lecture theatre, committee and common rooms, and a dining hall. A grant of £22,000 was made to Mr. Wylie McKissock, neurological surgeon at St. George's Hospital, London, for surgical research into anatomical and biochemical aspects of hemorrhage of the brain.

A grant of £10,000 to the Royal Geographical Society is to be used during 1960–63 to encourage participation of young people in exploration. Miscellaneous grants include £2,500 to the Crofters' Commission, £4,631 to the British Museum to acquire a sculpture, discovered at Nineveh, showing Babylonian prisoners being carried off by the Assyrians, and £2,500 to the Justice Educational and Research Trust for an inquiry into the investigation of complaints against administrative and executive decisions.

* Report of the Wolfson Foundation, 1955–1960. Pp. 39 (8 plates). (London: The Wolfson Foundation, 1960.)

PUBLICATION OF CALORIMETRIC AND THERMODYNAMIC DATA

THE "Resolution on Publication of Calorimetric and Thermodynamic Data", which was adopted by the fifteenth Calorimetry Conference held at Gatlinburg, Tennessee, during September 7–10, 1960, is a revised and extended form of the similar resolution adopted by the eighth Calorimetry Conference held in 1953. It outlines minimum publication standards for the guidance of authors, editors and referees of articles on calorimetry, and states the author's first responsibility is to report his results in a form related as closely as possible to the experimentally observed quantities, with enough details of the experiments and auxiliary information to characterize the results completely. Derived or secondary data should never be published without the primary data on which they are based. The auxiliary information should include a complete description of the apparatus and procedures, with details of the reaction vessel or calorimeter, the temperature and time measuring systems, the calibration and sensitivity of the instrument used and the precision and accuracy of the results obtained; the source and method of preparation of the samples studied, together with analyses and criteria of purity; and the values of the units and physical constants used in the calculations.

One section of the resolution deals in some detail with the presentation of results, and gives recommendations for the thermochemical data, thermal data, and calculated thermodynamic functions which should be included in the description of certain important kinds of thermodynamic studies. It is pointed out that graphical or analytical representation of results is sometimes worth while for the convenience of the reader, but such representations seldom are a satisfactory substitute for tabular presentation of accurate experimental results. Where rough measurements made for technical purposes, or measurements on materials of undefined composition or by inferior techniques, are reported, they should be given minimum journal space and the presentation should clearly recognize the lack of reliability of the results.

PROTEIN AND RIBONUCLEIC ACID IN THE GROWTH OF FERN GAMETOPHYTES

IN many Polypodiaceae, the germinating spore yields a filamentous protonema and rhizoid cell, that is, a 'one-dimensional' growth. After a certain time-lapse, the growing protonema begins to divide by longitudinal walls also, thereby yielding a plate-like structure, or 'two-dimensional' system. This leads on to the typical heart-shaped prothallus or gametophyte. Y. Hotta (*Jap. J. Bot.*, **17**, 214; 1960) has now contributed new facts about the role of protein and ribonucleic acid in the differentiation of the gametophyte of *Drygopteris erythrosora*.

Estimation of the protein contents during the course of development clearly indicates that whenever the two-dimensional growth takes place, a sharp increase in protein concentration in the cell can be observed, whereas in the course of the primary one-dimensional growth, protein concentration is gradually lowered. The two-dimensional growth can be specifically inhibited by some amino-acid analogues such as ethionine and 5-methyltryptophan, and is converted to the 'artificial' one-dimensional growth.

The same selective interference of the two-dimensional growth is also brought about by 8-aza-guanine, the effective inhibitor of the nucleic acid synthesis. This inhibition can be alleviated by adding corresponding amino-acids or guanine, respectively. Regardless of the nature of the effective inhibitors used, the selective inhibition is always accompanied by an immediate cessation of increase in the protein concentration followed by its gradual decrease. The author has also shown that ribonucleic acid from the two-dimensional prothallium possesses a nucleotide composition distinct from that in the one-dimensional growth. Ribonucleic acid found in the latter, induced artificially by 8-aza-guanine, has been shown to have practically the same nucleotide composition as that of the primary one-dimensional growth. Accordingly, it has been tentatively inferred that a special ribonucleic acid fraction which is sensitive to the action of 8-aza-guanine is closely related to the two-dimensional growth.

VIBRATIONALLY EXCITED NITRIC OXIDE PRODUCED IN THE FLASH PHOTOLYSIS OF NITROSYL CHLORIDE

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WHENEVER a molecule dissociates by absorbing radiation of shorter wave-length than is required from the known strength of the bond broken, the problem arises of the distribution of the excess energy among the fragments. Frequently it can be shown that one or more of these fragments are produced in an electronically excited state, but, in general, there is some energy which must appear in other forms. For a diatomic molecule, it follows that the atoms are produced with excess kinetic energy, but where a polyatomic molecule is concerned, there is the possibility that one or more of the products are produced vibrationally or rotationally excited in the ground electronic state. The present communication describes what seems to be the only direct experimental evidence that these possibilities are, in fact, realized.

In the flash photolysis of sulphur trioxide, Norrish and Oldershaw[1] observed the presence of vibrationally excited SO with $v'' \leqslant 3$, but, though it was shown that the effect was not thermal, it was not possible to decide whether the excited molecule was produced by primary photodissociation or by secondary reactions, that is:

$$SO_3 + h\nu \rightarrow SO^* + O_2 \qquad (1)$$

or

$$SO_2 + h\nu \rightarrow SO_2 + O(^1D) \qquad (2a)$$

followed by

$$O(^1D) + SO_2 \rightarrow SO^* + O_2 \qquad (2b)$$

Similarly, in the flash photolysis of nitrogen dioxide, Basco and Norrish[2] observed the first vibrationally excited level of nitric oxide, but again it was not possible to decide whether it is a primary or secondary product, in the latter case derived from:

$$O + NO_2 \rightarrow NO^* + O_2 \qquad (3)$$

We have now studied the flash photolysis of nitrosyl chloride in the presence of a great excess of inert gas to ensure isothermal conditions and have demonstrated the presence of very highly vibrationally excited nitric oxide. Many absorption bands in the region 2100–4000 Å. have been observed and it has been possible to assign most of them to transitions from the ground state of NO ($X^2\Pi_r$) to the $A^2\Sigma$, $B^2\Pi$, $C^2\Pi$ and $D^2\Sigma$ excited states and thus to demonstrate that all vibrational levels of the ground state up to $v'' = 10$ are populated. Some bands remain unassigned or only tentatively so, but it seems likely that these also will be found to correspond to transitions from vibrationally excited levels of the ground electronic state of NO. The decay of the excited molecules is very rapid and those in the higher vibrational levels are only present in appreciable concentrations during the photolytic flash.

Nitrosyl chloride can be decomposed by light of wave-length below about 6400 Å.[3] and, even at this wave-length, there is a slight excess of energy over that required to break the ON—Cl bond. Its extinction coefficient in the ultra-violet below 3350 Å. increases towards a maximum at around 1970 Å.[4] and, under the conditions obtaining in the experiments reported here, most of the absorption occurs

in the region below approximately 2700 Å. Assuming the transmission of the quartz flash-lamp and the reaction vessel is negligible below about 1950 Å. the excess energy available lies between about 70 kcal. and 110 kcal. It is now evident from our spectra that at least 50 kcal. of this excess energy can appear as vibrational energy of the nitric oxide molecule and we suggest that it is in the primary process :

$$NOCl + h\nu \rightarrow NO^* + Cl \qquad (4)$$

that this occurs.

The possibility that the NO is initially produced in an electronically excited state from which it enters vibrationally excited levels of the ground state has also been considered. This seems unlikely as there is no known electronic state of NO which, on spin conservation and energetic grounds, could qualify. Experiments designed to set an upper energy limit for this hypothetical electronic state are in progress, with particular reference to the $^4\Pi$ state predicted by Mulliken[5] to lie 4·5 eV. above the ground state.

It is also theoretically possible that NO produced initially without excitation could be excited by the flash. In the flash photolysis of NO this excitation has been realized[6], but it was shown that the reaction :

$$NO^2\Pi(v = 0) + h\nu \rightarrow NO^2\Sigma(v = 0, 1) \qquad (5)$$

followed by

$$NO^2\Sigma(v = 0, 1) + M \rightarrow NO^2\Pi(v = 0, 1, 2 \ldots) \quad (6a)$$

or

$$NO^2\Sigma(v = 0, 1) \rightarrow NO^2\Pi(v = 0, 1, 2 \ldots) + h\nu \quad (6b)$$

only produces an appreciable concentration of the first excited level, with the second only just detectable under favourable conditions. It follows that this mechanism can be excluded.

Two other reactions, namely :

$$NOCl + Cl \rightarrow NO^* + Cl_2 \qquad (7)$$

and

$$2Cl + NO \rightarrow NO^* + Cl_2 \qquad (8)$$

can be excluded by virtue of the fact that, when chlorine was photolysed in the presence of NOCl using a 'Pyrex' glass filter virtually to exclude the direct photolysis of NOCl, NO* was not observed. For the higher levels, the former can also be excluded on energetic grounds.

There is convincing evidence[7,8] that in exothermic reactions of the type :

$$A + BCD \rightarrow AB + CD \qquad (9)$$

up to 100 per cent of the energy liberated can appear as vibrational energy of the newly formed molecule *AB*. Reactions (2*b*) and (3) have provided the only indication so far that the molecule *CD* may be vibrationally excited to some extent ; but the fact that reaction (7) does not produce a detectable concentration of NO* militates against this. As there is no evidence for the presence of Cl_2* here or for O_2* being produced in reaction (2*b*), the question remains open.

If it be admitted that the primary process is :

$$NOCl + h\nu \rightarrow NOCl^* \qquad (10)$$

rather than direct photodissociation, two other possibilities exist, namely :

$$NOCl^* + NOCl \rightarrow NO^* + NO + Cl_2 \qquad (11)$$

and

$$NOCl^* + NO \rightarrow NO^* + NOCl \qquad (12)$$

Reaction (10) was proposed by Kistiakowsky[9] for decomposition at longer wave-lengths on the grounds that the absorption spectrum showed bands with line structure and that decomposition of NOCl could be achieved by light below 6400 Å., whereas the heat of dissociation (taken as 46·4 kcal.) corresponded to light below 6130 Å. The latter reason is invalid if the value of 37–38 kcal. is taken for the NO—Cl bond[9,10] and, as both he and Allmand[11] pointed out, the fact that the quantum yield of 2 for photolytic decomposition of NOCl is not reduced by a seven-fold dilution with nitrogen or a nine-fold reduction in pressure indicates primary dissociation. At the shorter wave-lengths this would appear to be even more likely. In the present work the excess of nitrogen as coolant over nitrosyl chloride and the pressure of nitrosyl chloride itself have each been varied by a factor of more than 100 without producing any fundamental change in the results obtained. It has also been shown that addition of small quantities of NO to NOCl produces no major effects. Larger quantities decrease the population of the higher levels, though they seem to increase that of the lowest excited level probably because of the reactions :

$$NO(v = n) + NO(v = 0) \rightarrow NO(v = n - 1) + NO(v = 1) \qquad (13)$$

To summarize, it appears likely that only reaction (4) could reasonably be expected to produce vibrationally excited NO in the yields obtained. The question arises as to the generality of this reaction ; but at least it can be said that the present evidence lends plausibility to reaction (1) and the corresponding reaction with NO_2. In the production of O_2* by the flash photolysis of ozone[12], the evidence for the mechanism :

$$O_3 + h\nu \rightarrow O_2 + O(^1D) \qquad (14)$$

and

$$O(^1D) + O_3 \rightarrow O_2^* + O_2 \qquad (15)$$

is convincing, though the possibility of a contribution from the reaction :

$$O_3 + h\nu \rightarrow O_2^* + O \qquad (16)$$

cannot now be excluded.

In preliminary experiments it was found that mixtures of nitric oxide and bromine, on standing for a short while, develop a continuous absorption spectrum in the ultra-violet which may reasonably be attributed to NOBr. Results generally similar to those with NOCl were obtained on flashing this mixture.

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IN VITRO TRANSFORMATION OF NORMAL CELLS BY POLYOMA VIRUS

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THE polyoma virus[1] provides favourable material for investigating the relationship between the lytic and the non-lytic interaction of a virus with animal cells, and for studying the cellular transformation which results in the development of tumours. A necessary requirement for such studies is the establishment of *in vitro* systems of analysis. It has been shown, in an *in vitro* system, that the lytic interaction of polyoma resembles that of some other viruses that do not produce tumours[2]; and it was further found that after *in vitro* infection of normal mouse embryo cultures it is possible to establish a line of cells with a stable cell-virus association[3]. The present experiments were undertaken in order to determine the consequences of infection of mouse kidney cells, and to develop for rat and hamster cells an *in vitro* system for the non-lytic transformation that results in the development of tumours. Rat and hamster tumours are rapidly produced by polyoma *in vivo*[4], and *in vitro* infection of normal embryo and kidney cells of these species showed no obvious cytopathic effect under conditions that produced a clear cytopathic effect on normal mouse cells.

Kidneys were used for the mouse experiments, since cells from this organ are very susceptible to tumour induction *in vivo*. In the first experiments, cultures were made of trypsin-dispersed kidney cells from 12-day-old mice that had been inoculated subcutaneously with polyoma virus *in vivo* when 2 days old. The cultures were seeded with 2×10^6 cells in 50-mm. Petri dishes with 4 ml. of medium consisting of 0·5 per cent lactalbumin hydrolysate in Earle's saline (*LA*-medium) and 10 per cent horse serum. The entire medium was charged every 2 or 3 days. These cultures formed monolayers, but at 5–6 days after seeding there was a strong cytopathic effect, and there was generally at this time virus with a haemagglutination titre of 8,092 per ml. in the culture fluid. It was also found at this time that, in addition to the cytopathic effect, there were groups of proliferating fusiform cells that did not undergo lysis despite the high virus titre in the medium. These cells were therefore presumably resistant to lysis by superinfection, in the same way as cells of the line that had been established from mouse embryo cultures[3].

The proliferating cells in the kidney cultures continued to grow and could form monolayers. But there were always some cells in the population that lysed, so that continued growth was dependent on the balance between cells that lysed and those that continued to divide. There was the same sequence of events in kidney cultures from 4-day-old mice inoculated with virus *in vivo* when 2 days old, and in monolayers of normal kidney cells from 7 to 10-day-old mice infected *in vitro* at a virus to cell ratio of 10 plaque-forming units per cell. The initial number of proliferating cells from mouse kidney cultures infected *in vitro* was much higher than in comparable experiments with mouse embryo cultures. The existence of proliferation and a lytic response in cells from the same organ has also been observed in organ cultures of mouse salivary glands[5].

Proliferation and lysis were found in all the kidney cultures, which were maintained for 1 month, and even in the line of mouse embryo cells[3] there was still some lysis after more than 1 year *in vitro*. The frequency of lysis seemed to depend on nutritional conditions, and in the mouse embryo line there was, after 1 year, no obvious lysis if the medium was charged daily, but a clear cytopathic effect if there was no change of medium for 3 days. It has been postulated that the non-lytic interaction of polyoma may be associated with the establishment of a provirus[6]. The detection of the non-lytic interaction in the mouse may, however, be complicated by the possibility that there may be a cytopathic effect as the result of lysis due to unstable conditions as in bacterial lysogeny[7], and/or to virus induction. The direct evidence for induction of polyoma virus will be discussed elsewhere (Winocour, E., and Sachs, L., unpublished work).

Kidney and embryo cultures were used for the rat and hamster experiments. Although rat cells could be satisfactorily cultured with *LA*-medium and 10 per cent horse serum, with this medium there was an early degeneration of hamster cultures. However, hamster cells could be grown in Eagle's medium with 4-fold concentration of amino-acids and vitamins (*EM*-medium) and horse serum, and grew even better in *EM*-medium and calf serum. 2×10^6 trypsin-dispersed cells from rat and hamster embryos, and kidneys of 7–9-day-old animals, and from hamster kidneys of adult (2–3 months old) animals were seeded in 50-mm. Petri dishes with 4 ml. of culture medium. The cultures were infected after 2–4 days, at a virus to cell ratio of 1 to 2 plaque-forming units per cell. Virus was adsorbed for 1 or 2 hr., and the possibility of different nutritional requirements for transformation was tested by using different media.

Following the assumption that the non-lytic interaction may be associated with the establishment of a provirus, it was further assumed that there might be another analogy to bacterial lysogeny, in that the frequency of the non-lytic transformation might be increased by the use of lower temperatures during the stages leading to the incorporative interaction[7]. Infected cultures with their controls were therefore also kept for various periods, after the initial seeding, growth and virus adsorption at 37° C., in an incubator with a humidified atmosphere and a constant flow of carbon dioxide in air maintained at 24° C. and then transferred again to an incubator maintained at 37° C.

Some representative results of the rat and hamster experiments are given in Table 1. The results show that non-lytic cellular transformations (as described later) can be obtained in rat and hamster after *in vitro* infection with polyoma virus. The transformations were dependent on the cultural conditions

Table 1. Cell Transformations and Acidity in Rat and Hamster Cultures infected with Polyoma Virus *in vitro*

Tissue	Exp. No.	Time at 24° C. (days)	Medium	Morphological transformation observed	Acidity
Rat embryo	126†	0	*EM–HOS*	+	+
	126	0	*EM–CAS*	−	+
	117*	0	*LA–HOS* or *CAS*	−	−
	132*	7	*LA–HOS* or *CAS*	+	+
	132	7	*EM–HOS*	−	+
	125	5	*EM–CAS*	−	+
Rat young kidney	123*	0	*EM–HOS*	−	−
	123	0	*EM–CAS*	−	±
	123	7	*EM–HOS*	−	−
	123	7	*LA–HOS*	+	+
Hamster embryo	131*	0	*EM–HOS*	−	±
	131	0	*EM–CAS*	−	+
	131	8	*EM–HOS*	+	+
	130†	8	*EM–CAS*	+	+
Hamster young kidney	127*	0	*EM–CAS*	−	+
	127	7	*EM–HOS*	+	+
	128†	7	*EM–CAS*	+	+
Hamster adult kidney	122*	0	*EM–HOS*	−	−
	122	0	*EM–CAS*	−	+
	122	5	*EM–HOS*	+	+

EM., Eagle's medium with four-fold concentration of amino-acids and vitamins; *LA*, 0·5 per cent lactalbumin hydrolysate in Earle's saline; *HOS*, horse serum; *CAS*, calf serum, 10 per cent serum.

Col. 5: +, transformation; −, no difference observed between infected and control.

Col. 6: +, strong colour difference between infected and control; ±, slight colour difference; −, no colour difference.

* Entire medium changed every 3 or 4 days.

† No change of medium after virus infection.

and the medium used. Thus, for example, with respect to morphological changes, no transformation was observed (exp. 132) in rat embryo cultures with 7 days at 24° C. in *EM*-medium and horse serum, whereas there was a clear transformation under the same cultural conditions with *LA*-medium and horse serum. In the hamster embryos (exp. 131) transformation was observed with calf but not with horse serum, in cultures maintained only at 37° C., whereas transformation with horse serum was found in cultures kept at 24° C. for 8 days after infection. Preliminary experiments on different times at 24° C. indicated that 5–8 days was a suitable time, and transformation was observed in all tissues with the appropriate medium maintained at 24° C. for this period. It also appeared that there was a clearer transformation with a longer time-interval between medium changes. The transformations were observed between 9 and 14 days after infection, and experiments were terminated at 17–26 days.

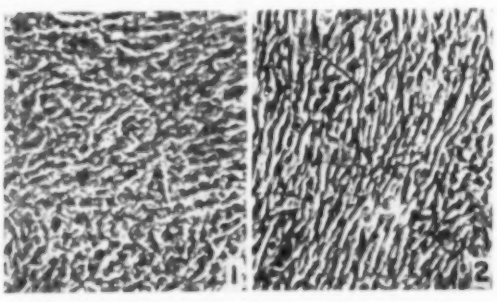

Fig. 1. Control culture of rat embryo cells. Fig. 2. Culture of rat embryo cells with fusiform transformation. Fourteen days after *in vitro* infection with polyoma virus. Methanol fixation, unstained, phase contrast. (× *c*. 112)

In some experiments, in both rat and hamster, there was a regular transformation to fusiform cells (Figs. 1 and 2). In other experiments, with hamsters, fusiform cells tended to form strands with the cells piling up on one another. The difference in appearance of the transformed cultures may have been due to the different conditions under which the cells were grown. The piling-up observed was similar to that produced after *in vitro* infection with Rous sarcoma virus[8]. The transformation by tumour viruses thus presumably includes a loss of contact inhibition[9]. The observation of a transformation is, of course, dependent on a recognizable difference from non-infected control cultures, and in some cases morphological changes may have occurred in infected cells which were not sufficiently different from the controls to be detected readily in the living cultures.

In addition to the morphological changes, there was a difference in the acidity of the medium, in that the transformed cultures were obviously more acid than their controls. There were also some cases (Table 1) of a more acid medium in infected cultures without a morphological difference from the controls. The difference in acidity is presumably due to the changed metabolism of transformed cells. A further difference in both rat and hamster was the better survival of infected cultures under conditions where the controls degenerated. There was also in some experiments a better growth in infected cultures where the controls did not degenerate; and a difference in response to trypsinization. During trypsinization, the cells of controls readily formed cell suspensions, whereas the infected cultures came off the glass either with difficulty and/or in clumps that did not readily disperse.

The above experiments have shown that, in addition to an *in vitro* system for the study of the lytic interaction with polyoma virus, a suitable system is now available for the *in vitro* analysis of the non-lytic interaction associated with cellular transformation. Since the *in vitro* transformations observed include changes in cell morphology, cell metabolism, and what is presumably a loss of contact inhibition, the question arises whether all these changes are required for the malignant transformation. Experiments are therefore now in progress on the growth of the cell cultures in animals.

Note added in proof: Since the above was written, progressive growth has been obtained after inoculation of *in vitro* transformed hamster cells (taken at 14–16 days after *in vitro* infection) into adult hamsters, thus showing that these cells were neoplastic when tested *in vivo*. An independent finding of *in vitro* transformation of hamster embryo cells has also recently been reported[10].

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CARBONIC ANHYDRASE AND THE INNER EAR

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THE finding of carbonic anhydrase in the ciliary body[1] and in the choroid plexus[2] initiated a long series of experiments involving the activity of this enzyme in the secretion of the aqueous humour and cerebrospinal fluid, and also in the treatment of glaucoma and hydrocephalus[3,4]. We were prompted by results from those experiments to search for carbonic anhydrase in the tissues of the inner ear, and to see what effects the specific inhibitor acetazolamide ('Diamox') might have on the composition of the endolymph.

Seventeen cats, initially anæsthetized with sodium pentobarbital (42 mgm./kgm. intraperitoneally), were used. The middle ear was approached from the ventral side, the bulla was removed and samples of perilymph and endolymph were taken using the approach and technique described by Aldred, Hallpike and Ledoux[5]. In twelve experiments, the fluid was collected by means of capillary tubes; the fluid was then put into small test-tubes and 5-λ samples were taken by ultra-microscopic pipettes. In the remaining experiments the capillary tubes were weighed before the samples were taken, again after sampling, and the volumes were calculated from the weights. After the samples had been taken, the tissues were dissected out under $\times 40$ magnification of the microscope. The apical, middle and basal turns of the cochlea, the vestibule (comprising mainly utricle, saccule, ampullæ and the anterior semicircular canal) and the saccus endolymphaticus, which was approached posteriorly, were all removed and analysed for carbonic anhydrase by the method of Maren, Ash and Bailey[6]. The results of these analyses, compared with those from other tissues in the cat[2], are shown in Table 1. These results, taken with earlier estimations in a variety of tissues[7], gave the surprising result that the tissues of the cochlear partition possess the highest known concentrations of carbonic anhydrase activity of any organ assayed.

There appeared to be a specific distribution of enzyme, with the highest concentrations in the apical turn and saccus endolymphaticus, progressively lower concentrations in the middle and basal turns, and lowest concentrations in the vestibule (Table 1). The striking difference between the carbonic anhydrase concentrations of the cochlea and vestibule deserves comment here. The explanation of the differences may lie in the cytological differences found by Smith[8] in the epithelial cells of the stria vascularis and of the vestibule. Pease[9] showed that organs active in the transfer of fluid are characterized by a great increase in the basal cell surface, and that in kidney tubules, submaxillary gland, choroid plexus, and ciliary body, intensive folding of the basal plasma membrane occurs. All these organs have high concentrations of carbonic anhydrase. Similar structural characteristics have been found to be present by Smith in the utricle[10] and in the stria vascularis and spiral prominence[8]. The stria vascularis, however, is a unique structure in the entire membranous labyrinth. On the other hand, it seems certain that endolymph must be formed and absorbed in the vestibule as well as in the cochlea. Smith[8] suggests that transfer of fluid may be more rapid in the stria vascularis, but also that "the cytological specialization of the marginal cells" of the stria vascularis "suggests some additional process and the question arises whether it may not be also the site of some activity specific to the cochlea". This "cytological specialization" consists of beaded vesicles found in abundance in the basal portions of the marginal cells of the stria vascularis. Palade[11] has observed them in macrophages and suggested that they may be a route for pinocytosis and phagocytosis. One cannot help but speculate that this specialization may be concerned in some way with carbonic anhydrase activity, and that the vesicles may represent sites of concentration of the enzyme.

Control electrolyte data were compiled on plasma, cerebrospinal fluid, perilymph and cochlear endolymph (Table 2). In general these conform closely to the data previously reported by others[12–14]. In confirmation of the work of Smith *et al.*[12], and of Citron and Exley[13], we have found high concentrations of potassium in the endolymph, although this is clearly subject to considerable individual variation. Both these groups have also reported wide ranges of potassium concentration in the cochlear endolymph, but have presumed that the lower values must be artefactual in their origin. The data given by Citron and Exley[13] are presented in Table 3 with their reasons for the values of endolymph potassium. They report that it was the Na^+ and K^+ concentrations *per se* of the endolymph in many samples which suggested contamination with perilymph, and only three samples showed the high values given in the table. In our experiments (Table 3) there are numerous possible reasons for this variation: the difficulty of sampling less than 5λ of fluid, the magnitude of volumetric error, and contamination from perilymph, especially in view of the fact that we do not have any histological sections of this material; it may also be that the potassium concentration of the endolymph is subject to considerable variation physiologically, similarly

Table 1

Tissue	Species	Enzyme units/gm. wet tissue
Choroid plexus (ref. 2)	Cat	262
Kidney (ref. 2)	Cat	275
Ciliary process (ref. 1)	Rabbit	30
Whole blood (ref. 2)	Cat	950
Whole blood (present study)	Cat	943
Inner ear (present study)		
Basal turn	Cat	1,086 ± 314
Basal + middle turns	Cat	1,470
Middle turn	Cat	2,263 ± 556
Apex + middle turn	Cat	2,380
Apex	Cat	3,162 ± 1,180
Saccus endolymphaticus	Cat	3,000
Vestibule	Cat	81 ± 17

Concentration of carbonic anhydrase in inner ear and other tissues. Data obtained from six cats. In two cats, it was impossible to separate middle from basal and apical turns. Only two cats yielded data on the saccus endolymphaticus.

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Table 2

	Before acetazolamide				After acetazolamide			
	Plasma	Cerebrospinal fluid	Perilymph	Endolymph	Plasma	Cerebrospinal fluid	Perilymph	Endolymph
CO_2 mM/l.	17·2 (9)	21·1 (4)	16·9 (7)	18·6 (5)	11·8 (8)	21·4 (1)	17·6 (2)	—
Cl^- mM/l.	120·5 (9)	133·4 (4)	143·4 (6)	157·2 (2)	120·0 (8)	137·1 (1)	158·5 (4)	140·7 (4)
K^+ mM/l.	4·3 (6)	4·5 (2)	7·9 (6)	67 (7)	3·6 (8)	3·7 (1)	6·2 (7)	15 (7)

Mean carbon dioxide, chloride and potassium concentrations before and 6–8 hr. after administration of acetazolamide (see text). Numerals in brackets indicate sample number of animals used. For fuller details of potassium concentrations in endolymph see Table 3.

to the potassium concentration of the urine, which is also dependent on a secretory mechanism. It is, however, evident from the data of all workers that potassium is the chief cation of the endolymph, and presumably this unique characteristic reflects the secretory activity of the cells of the cochlear partition. The large variation in K^+ concentration must at present remain unexplained.

Potassium concentration of the perilymph ranged from 6–11 m.equiv. except in one sample, which contained 32 m.equiv.

In six cats, acetazolamide was given intravenously (50 mgm./kgm. as the sodium salt) at zero time and again six hours later, followed by the same dose given intraperitoneally after 12 hr. In some cases pentobarbital anæsthesia was used to facilitate the intravenous injection. 15 hr. following the initial injection of acetazolamide, the dissection procedures described here were carried out. In five experiments, samples were taken from the inner ear of one side in the normal anæsthetized cat. 50 mgm./kgm. acetazolamide was then given intravenously, and 3 hr. later samples were taken from the other ear. Electrolyte and drug concentrations were then determined.

At the time of removal of the samples, the plasma concentrations of acetazolamide ranged from 17 to 65 µgm./ml. The tissues of the inner ear were found to contain drug in the same range, averaging 30 µgm./gm. of tissue or 2×10^{-4} molar. From the values of enzyme units given in Table 1 and the corresponding molar concentrations of enzyme (E) which may be computed from other work in this laboratory[15], it is found that the enzyme concentration in these tissues ranged from about 1 to 6×10^{-5} molar. The K_I of acetazolamide is approximately 1×10^{-8} molar. From these values it may be calculated that the concentrations of acetazolamide found in the tissues are enough to inhibit more than 99·9 per cent of the enzyme originally present.

It was of interest in these experiments that, following the administration of acetazolamide, the volumes and pressures in the perilymph and endolymph appeared considerably reduced, a situation comparable to that reported for cerebrospinal fluid[4] and aqueous humour[1].

Carbon dioxide. The typical renal effect of acetazolamide was elicited, and the animals, at the time the samples were taken, had a definite metabolic acidosis. While untreated cats in the series had average total carbon dioxide values in plasma of 17 mM/l., after drug administration the values dropped to 11 mM/l. In five normal cats, values for the carbon dioxide of the endolymph ranged from 15 to 21 mM/l., and were not significantly different from those of the plasma and cerebrospinal fluid simultaneously sampled.

Chloride. Results for endolymph are preliminary in nature since only six samples were obtained. In two normal samples, the concentration of chloride in the endolymph was higher than that of the perilymph. Our results suggest that following acetazolamide, endolymph chloride decreased, while perilymph chloride may have increased. There does not appear to be any significant change in chloride concentration in either the plasma or the cerebrospinal fluid.

Potassium. Administration of acetazolamide appeared to eliminate all the high values of potassium concentration in the endolymph, and gave average potassium ion values which are strikingly less than the overall values of endolymph reported in our controls and for those of the workers previously cited (Table 3).

Perilymph potassium concentrations following the drug (Table 2) were in the same range as those from control animals. In the few cases studied, the values for cerebrospinal fluid were in the normal range.

These results suggest that carbonic anhydrase may play an important part in the mechanism of active secretion of potassium into the endolymph, and possibly in the overall formation of this fluid. In view of current theories regarding the etiology of Ménière's disease as a 'hydrops' of the inner ear, the obvious analogy to hydrocephalus and glaucoma suggests a rational basis for a controlled trial of acetazolamide for this syndrome.

Table 3

Ref. 13. Cat	
Potassium	117·0 (12)*

* In many of these samples the sodium and potassium concentrations suggested contaminations with perilymph. Three samples, however, showed the high values for potassium given in the table. The bracketed figure appended to each entry represents the total number of observations on which it is based.

Present study cat	
Controls	9, 20, 51, 55, 85, 123, 127 Av. = 67
15 hr. after acetazolamide	15, 21, 13, 2, 16*, 26†, 10† Av. = 15

Potassium concentration in cochlear endolymph (m.equiv./l.) of cat.
* 3 hr. cat; † 6 hr. cat.

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LABILITY OF N-*o*-CARBOXYPHENYLRIBOSYLAMINE AS A FACTOR IN THE STUDY OF TRYPTOPHAN BIOSYNTHESIS

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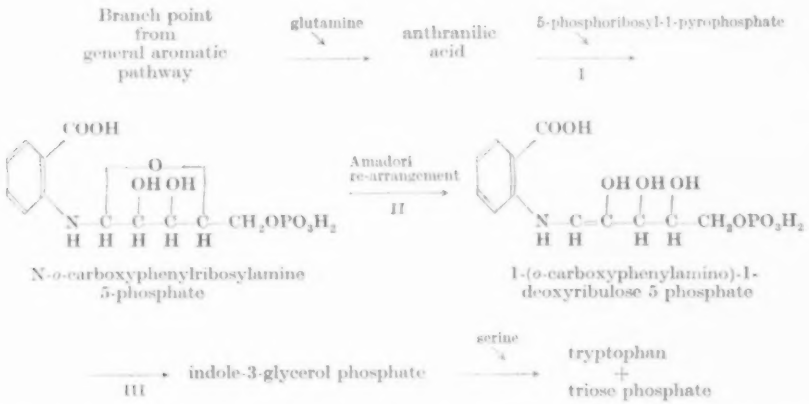
INVESTIGATIONS with both whole cells[1] and cell extracts[2] have established 1-(*o*-carboxyphenylamino)-1-deoxyribulose 5-phosphate as an intermediate in tryptophan biosynthesis. The likely sequence of reactions is:



The relation of anthranilic acid to tryptophan biosynthesis has recently been discussed in some detail[3]. Mutants blocked in reaction II would normally be expected to excrete N-*o*-carboxyphenylribosylamine (the dephosphorylated form of the postulated intermediate), but preliminary data based on the Bratton and Marshall[4] colour reaction suggested that spontaneous hydrolysis would result in the accumulation of large quantities of anthranilic acid. In this event such mutants would appear to be blocked in reaction I.

Since the Bratton and Marshall method requires the use of acid conditions which could favour the formation of artefact anthranilic acid, the lability factor was re-examined by a new method not requiring the manipulation of *p*H.

In Fig. 1 the ultra-violet absorption spectrum of anthranilic acid is compared with that of N-*o*-carboxyphenylribosylamine under equivalent conditions in a typical biological medium. Since the differential at 247 mμ is present over the *p*H range 6·0–9·0, this was used to follow the reaction: N-*o*-carboxyphenylribosylamine $\xrightarrow{H^+}$ anthranilic acid without the necessity of adjusting the *p*H of experimental samples. The general method was as follows. A 0·005 *M* solution of N-*o*-carboxyphenylribosylamine (or other anthranilic acid glycosylamine) was prepared in 0·05 *M tris* buffer, *p*H 9·0. A 1-ml. portion of this solution was added to 49 ml. of experimental buffer (for experiments at 37° this was pre-heated) to give a final glycosylamine concentration of 0·0001 *M*. The zero-time sample was withdrawn immediately and the bulk of solution placed in a water-bath at the experimental temperature. Further samples were withdrawn as required. The absorbance of all samples was read at 247 mμ (ultra-violet spectrophotometer) without delay.

For the *p*H range 6·0–7·0 the experimental buffer was Davis minimal medium[5] adjusted when necessary with potassium dihydrogen phosphate; in the range *p*H 7·5–9·0 the buffer was 0·1 *M tris*.

At 100 per cent conversion to anthranilic acid there was excellent agreement with the known overall ultra-violet absorption of anthranilic acid (Fig. 1), while at intermediate stages the spectra were consistent with the appropriate mixture of anthranilic acid and glycosylamine derivative.

As shown in Table 1, the half-life of N-*o*-carboxyphenylribosylamine is dependent on *p*H. Media used in accumulation studies with tryptophan auxotrophs are rarely buffered at *p*H-levels greater than 8. Unless special precautions are taken, the buffer is broken and it is not uncommon for the *p*H to fall to between 5 and 6. Even without this drop the

Table 1. STABILITY OF N-*o*-CARBOXYPHENYL-D-RIBOSYLAMINE (0·0001 *M*) AS A FUNCTION OF *p*H AT 37°

*p*H	Half-life (hr.)
6·0	0·1
7·0	0·5
7·8	2·1
8·0	3·2
8·4	6·0
9·0	20·0 (approx.)

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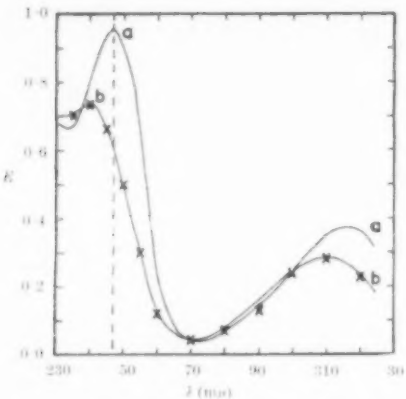

Fig. 1. Absorption spectra of : (*a*) N-*o*-carboxyphenyl-D-ribosylamine ; (*b*) anthranilic acid, both 0·0001 *M* in Davis minimal medium, *p*H 7·0. The analytical method for anthranilic acid in the presence of its glycosylamine derivatives depends on the differential at 247 mμ. This differential is essentially the same between *p*H 6 and *p*H 9 . . . absorption of (*a*) at 100 per cent hydrolysis to anthranilic acid determined by $E_{247\,m\mu}$

chemistry of the situation confirms that strains blocked in biosynthetic reaction II would form large quantities of anthranilic acid, a characteristic expected of strains blocked in reaction I. Strains blocked in reaction III are often referred to as anthranilic acid-accumulating strains. While mutants of this class do form anthranilic acid, appropriate examination of supernatants leaves no doubt that the Amadori derivative is the major product. In the case of mutants blocked in reactions I or II, anthranilic acid would appear as the major product of both types. Various experiments with whole cells[3] have not clarified the problem beyond a slight suggestion that mutants of type II might exist. It seems clear that whole cells are unsuitable for these investigations, principally because there is likely to be a permeability barrier to the phosphorylated glycosylamine. At the cell-free level the situation can be rationalized once the lability factor is taken into account. If both anthranilic acid and N-*o*-carboxyphenylribosylamine 5-phosphate are normal obligate intermediates, it is likely that tryptophan auxotrophs known to form anthranilic acid (in the strict sense discussed above) will eventually be shown to consist of two classes : (*a*) a class able to condense anthranilic acid with 5-phosphoribosyl-1-pyrophosphate ; (*b*) a class deficient in this respect. It is also possible that the Amadori re-arrangement step is non-enzymatic.

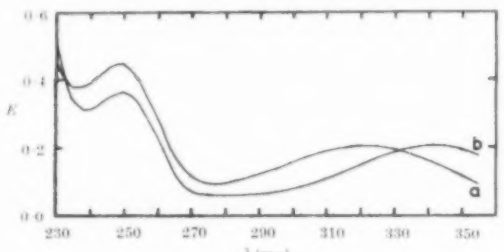

Fig. 2. Absorption spectra of crude 1-(*o*-carboxyphenylamino)-1-deoxy-D-ribulose 5-phosphate. (*a*) 0·0001 *M* in buffer *p*H 7·0 (potassium phosphates 0·1 *M*) ; (*b*) *p*H adjusted to < 2 with conc. hydrochloric acid

With cell extracts the lability factor to be considered is that of N-*o*-carboxyphenylribosylamine 5-phosphate, not that of the dephosphorylated artefact. The phosphorylated version has yet to be synthesized and is therefore not available for study. Unsuccessful syntheses (Doy, C. H., and Doy, F. A., unpublished) based on successful methods for the nonphosphorylated glycosylamines of anthranilic acid[1] suggest that the phosphorylated form is more labile. A dividend from this work was the isolation of a crystalline compound with properties expected for the phosphorylated Amadori intermediate, 1-(*o*-carboxyphenylamino)-1-deoxyribulose 5-phosphate. Although Doy and Gibson[4] and Smith and Yanofsky[2] have described preparations of the non-phosphorylated and phosphorylated Amadori compound, a crystalline product has not been isolated previously. The present product has yet to be completely characterized, but its ultra-violet absorption at 10^{-3} *M* (Fig. 2) has the expected characteristics. On the basis of previous work, the extinction is of the order predicted. In contrast, Smith and Yanofsky[2] describe similar absorption, but at 10^{-3} *M*. The present measurement is based on weighings calculated from the formula $HOOC.C_6H_4.NH.CH_2.CO.(CHOH)_2.CH_2OPO_3Na_2$, while Smith and Yanofsky base their spectrum on a concentration determined by enzymatic conversion to indoleglycerol phosphate. Since concentration based on weighing is more direct and impurity would be expected to shift maxima or depress extinction, the enzymatic data seems in some doubt.

The purely chemical observations suggest that N-*o*-carboxyphenylribosylamine 5-phosphate is (*a*) more easily hydrolysed to anthranilic acid than the non-phosphorylated form, and (*b*) easily converted to the Amadori compound. The first point would re-emphasize the lability factor in cell-free studies, and the second the possibility that the Amadori re-arrangement is non-enzymatic.

Since manipulations can be reduced to the minimum, fluorescence seems to be the most suitable means of looking for reaction I with cell-free systems. Methods which require the precipitation of protein with trichloracetic acid, or extraction procedures at acid *p*H, ignore the lability factor.

Smith and Yanofsky[2] have applied fluorometry to cell-free studies with anthranilic acid-accumulating tryptophan auxotrophs. Excluding those that were blocked immediately after the Amadori compound (Tryp-3*a* mutants), the remainder (Tryp-3*b* mutants) were classed as blocked immediately after anthranilic acid on the basis of failure to metabolize anthranilic acid. Since the reference describing the fluorometric method requires samples to be transferred to *p*H 6·0, it is possible that the lability factor has obscured the metabolism of anthranilic acid to its ribosylamine 5-phosphate. Similarly, experiments with radioactive substrates do not exclude the possibility of hydrolysis following enzymatic synthesis.

It is not clear whether 'mixing experiments' were done within the Tryp-3*b* class. If individual mutants within this class were point mutations lacking in one instance the enzyme necessary for reaction I and in another the enzyme necessary for reaction II, they would be expected to complement each other in the way described[2] for extract mixtures of Tryp-3*a* and Tryp-3*b* mutants. Such complementation would suggest a subdivision within class Tryp-3*b* mutants without the need to measure N-*o*-carboxyphenylribosylamine 5-phosphate directly.

If experiments can be designed which adequately account for glycosylamine lability, it should be possible to decide finally the question of whether some, all, or none of the anthranilic acid-accumulating strains are blocked in the Amadori re-arrangement step. It will then be easier to decide whether anthranilic acid has the status of a normal obligate intermediate.

This work was for the most part completed in the Bacteriology School, University of Melbourne, and supported by the Australian National Health and Medical Research Council. Work at Harvard was supported by a Fulbright Research Fellowship and a Commonwealth Scientific and Industrial Research Organization Overseas Post-Graduate award.

Note added in proof. Enzymatic results have now been obtained which are consistent with the division of anthranilic acid-accumulating mutants into a group blocked in reaction I and a group blocked in reaction II (Doy, C. H., Rivera, A., and Srinivasan, P. R., *Biochem. Biophys. Res. Comm.*, in the press).

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LOCATION OF THE NON-LINEARITY IN HORIZONTAL CELL RESPONSE TO RETINAL ILLUMINATION

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IN 1953, Svaetichin[1], using micropipette electrodes, found graded responses to light stimuli in isolated fish retinæ. Starting from a negative membrane potential of 10–50 mV., a graded hyperpolarizing signal, termed the 'luminosity response', could be obtained. The relationship between response and light intensity was found to be non-linear. As will be shown, it would appear that the receptor process is linear, and that the non-linearity is probably located in the region of a horizontal cell.

In recent work[2], we have definitely localized the site of origin of the luminosity response by the use of a marking technique[3] and subsequent histological examination. The response was found to originate in horizontal cells located in the bipolar cell layer of the retina. These cells are comparatively large, about 100μ across, and of quite low resistance (probably less than 100 kΩ (ref. 4)). On the basis of ultrastructural studies[5], these horizontal cells are considered to be glia, non-neuronal structures which are apparently much more permeable to sodium than to potassium[6]. Further, retinal tissue contains roughly equal amounts of sodium and potassium[7], neurons and glia are closely packed[5] (100-Å. spacing), and the 'extraneuronal' space is probably about equal to the neuronal space[6]. It is therefore likely that in glia cells the concentration of sodium must be considerably greater than that of potassium.

The non-linearity in horizontal cell response can be exhibited in two ways. Svaetichin *et al.*[8] showed that if the illumination per unit area is kept constant, but the illuminated area increased, the response increased with the number of cones thus illuminated, as shown in Fig. 1. It will be noticed that if the number of cones is not too small, the response increases as the logarithm of the number of cones. If the illuminated area remains constant, but the light intensity is increased, the response increases as the logarithm of the light intensity, provided the illumination is not too low. This is shown in Fig. 2. In this case a large number of cones were illuminated.

The fact that the curves in Figs. 1 and 2 have similar semi-logarithmic forms is explained by the following experimental result: The retina is illuminated by two light spots of the same diameter and of equal intensity, in one case overlapping, and in the other case just touching. The ratio of the response with two spots to that with one spot illuminated is found to be the same under both conditions. A typical result for Centropomidae is shown in Fig. 3, each spot illuminating about a hundred cones. In fact, if the two spots are non-overlapping and the effective intensity taken as the sum of the intensities of the

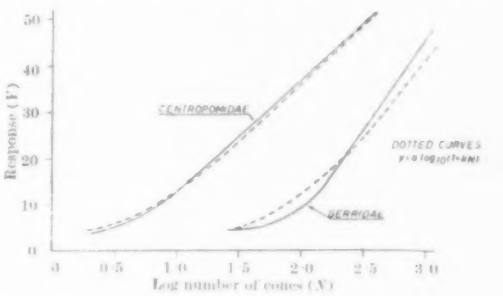

Fig. 1. Horizontal cell response as a function of the number of cones illuminated

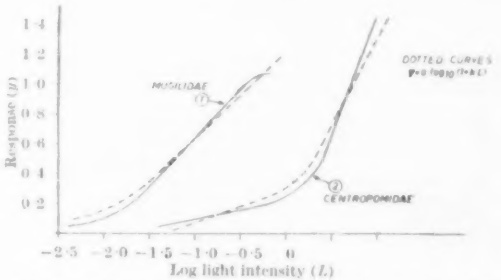

Fig. 2. Horizontal cell response as a function of the retinal illumination. Zero on the horizontal scale corresponds to different light intensity values for curves (1) and (2)

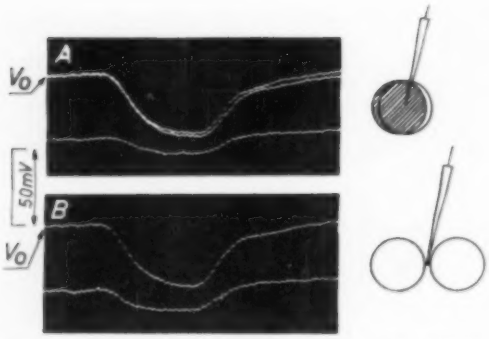

Fig. 3. Luminosity response in Centropomidae, overlapping (*A*) and adjacent (*B*) light spots of equal intensity. V_0 is resting potential of the horizontal cell. Duration of light stimulus is 350 msec. Top traces in (*A*) and (*B*) show response to single light spot; bottom traces show response with one spot permanently illuminated and the other switched on and off

two spots, the response is similar to the Centropomidae curve in Fig. 2. Hence, since two different groups of cones are involved when the light spots are separated, the non-linearity which affects the horizontal cell response cannot be in the receptors themselves, but must be where their signals converge. This is shown schematically in (*A*) of Fig. 4. Considering Fig. 1, it now follows that if the number of illuminated cones are increased from N_1 to N_2, with a fixed light flux per cone, the response is that which would be obtained by keeping the number of illuminated cones fixed at N_1 but increasing the illumination in the ratio N_2/N_1. Thus, the curves in Figs. 1 and 2 may be expected to have similar semi-logarithmic shapes, since Fig. 2 was obtained with a fixed light spot diameter.

The physiological system involved is more in accordance with (*B*) of Fig. 4, since the bipolars which receive signals from the receptors are in close proximity to the horizontal cell the electrical response of which is measured by means of a micro-electrode. It may therefore be expected that the non-linearity is subsequent to the summated actions of the bipolars on the horizontal cell. It is tempting to go further and assume that the horizontal cell potential is associated with a concentration difference of a particular ion i between the inside and the outside of the cell, the 'outside' of the cell being presumably the extremely narrow intercellular spaces of approximately 100 Å. width which are seen in high-resolution electronmicrographs[8]. The resting potential of the horizontal cell is then:

$$V_0 = A \log_{10} \frac{i_0}{i_i} \qquad (1)$$

where i_i and i_0 are respectively the inside and the outside concentrations of the ion i, and A is a constant.

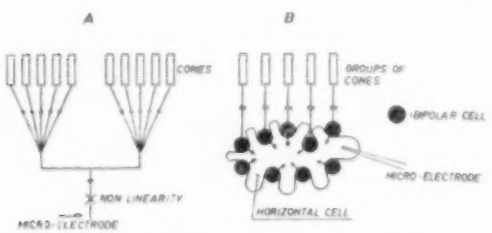

Fig. 4. Location of the non-linearity in horizontal cell response to retinal illumination

We assume that when the cones are illuminated, and equilibrium conditions have been established, a quantity of ions i proportional to the illumination L has passed from the bipolars into the horizontal cell. The horizontal cell potential is therefore increased to:

$$V_L = A \log_{10} \frac{i_0}{i_i + b.L} \qquad (2)$$

where b is a constant. It is assumed that the ion concentration i_0 in the 100 Å. intercellular space remains unchanged. Hence, the response to light, as measured by the change in resting potential, is:

$$V_L - V_0 = -A \log_{10}(1 + k.L) \qquad (3)$$

where k is a constant equal to b/i_i. The dotted curves in Figs. 1 and 2 are of the form given in equation (3), and there is at least a fair fit with the experimental results. However, there is difficulty in accepting this simple interpretation of the source of the non-linearity. The horizontal cell is large, about 100μ diameter, and diffusion of sodium or potassium ions throughout the cell would take a time of the order of 700 msec., using the Hodgkin and Keynes[9] measurements of diffusion-rates in squid axoplasm. But only about 50 msec. elapses between application of illumination and attainment of 80 per cent of the maximum response in the horizontal cell, a time which also includes transmission from the receptors to the bipolar cells (a distance of about 60μ in the fish). Possibly the ionic influx from the bipolars spreads along the cell in some way which involves electric field gradients. It is perhaps significant that if the fish is dark adapted, the luminosity response still follows a similar curve to equation (3); however, the response now has very slow rise and decay phases about 1 sec. (ref. 10), so that this may indicate a diffusion process. In any event, it would certainly appear that the non-linearity in response is closely connected with the horizontal cell; there is, at least, formal correspondence between the response and a hypothetical mechanism which involves the passage of ions between bipolars and the horizontal cell, and the associated change in ionic concentration ratio between the interior and the exterior of the horizontal cell.

Finally, it is interesting that the psychological scale of lightness[11] can be fitted quite well by a relationship of the form of equation (3), while it is well known that in the retina of fishes, etc., there are ganglion cell units where the relationship between spike frequency and illumination is also of a similar form. It is reasonable to suppose that the change of bipolar cell potential in response to light can be represented by equation (3), and that the spike frequency is linearly related to this graded potential as has been shown, for example, by Fuortes[12] in *Limulus*.

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FOUR ADULT HÆMOGLOBIN TYPES IN ONE PERSON

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THE normal adult type of human hæmoglobin (A) is a single molecular species with the chemical constitution $\alpha_2{}^A\beta_2{}^A$ (ref. 1). Such a molecule contains two identical α polypeptide chains and two identical β chains. It has been shown that the genetically controlled abnormal human hæmoglobins previously examined contain an abnormal α or an abnormal β chain, carrying an amino-acid substitution[2,3]; for example, lysine for glutamic acid in the β chain of hæmoglobin C, $\alpha_2{}^A\beta_2{}^C$ (ref. 4). We wish to report the results of chemical studies on four adult hæmoglobin components[5] found in a single individual, D. K. P.; her hæmoglobins turned out to be normal in both peptide chains, abnormal in one or other chain and abnormal in both chains, respectively. Apart from their genetic interest, these findings allow us to make certain deductions about the mode of assembly of the hæmoglobin molecule.

The blood sample from this patient, D. K. P., became available to us through the kindness of Dr. L. M. Tocantins and Miss J. Atwater of Philadelphia. They have already described[5] the occurrence of four hæmoglobins in approximately equal amounts in this blood, together with their clinical findings. The hæmoglobins are electrophoretically distinct at *p*H 8·6; they have been called[5] hæmoglobins A, G, C and X, which is the order of migration, with A as the fastest component. Electrophoretic comparison with authentic specimens is the basis for naming the first three hæmoglobins: hæmoglobin X was unknown and the slowest hæmoglobin yet described. The hæmoglobin G was found by these authors[5] to behave identically with a specimen of G from Dr. Schneider. It may therefore be identical with the hæmoglobin G of Lehmann and Edington[6] and with the G_{1b} (for G_{Ibadan}) recently described by Shooter *et al.*[7], and found by them to be abnormal in the α chain. On the other hand, D. K. P.'s hæmoglobin G is different from the G of Schwartz *et al.*[3,8] which carries a substitution of glycine for glutamic acid in the β peptide chain.

The original characterization of hæmoglobins A, G, C and X was done by paper electrophoresis[5]. We have been able to confirm the presence of the four components by starch-gel electrophoresis[9] at *p*H 8·6 in 0·02 *M* veronal buffer (see Fig. 1). The four proteins were also separated by electrophoresis on a starch block[10] in the same buffer. The relative amounts (per cent) recovered were: A, 35; G, 27; C, 23; X, 15.

Each hæmoglobin was digested with trypsin and fingerprinted[11]. Hæmoglobin A appeared to be completely normal (Fig. 2) and hæmoglobin C showed only the expected absence[4] of peptide 4 and its replacement by two new peptides, C-4*a* and C-4*b* (C-4*b* = hæmoglobin C tryptic peptide 4*b*). These peptides were isolated, hydrolysed and their amino-acid content analysed. The results confirmed the glutamic acid to lysine substitution previously reported for hæmoglobin C[4]. It appears, therefore, that D. K. P.'s hæmoglobin C is authentic hæmoglobin C.

Fingerprints[11] of D. K. P.'s hæmoglobin G were more difficult to interpret. The fingerprinting technique had to be modified to make it more sensitive. Isolated peptide bands from paper ionophoresis at *p*H 6·4 are compared side by side by a second ionophoresis on Whatman No. 3*MM* paper in a *p*H 4·7 buffer. It eventually appeared that in hæmoglobin G, two normal peptides—A-3 and A-9—had been replaced by three new peptides. No other changes have so far been detected.

The following relationship for these five peptides was established by means of quantitative amino-acid analyses of the isolated peptides with the Spinco model Moore and Stein automatic analyser, by end-group determinations with the dinitrophenol procedures[12], by stepwise degradation with the Edman–Sjoquist procedure[13] and by fingerprinting[11] of some of the peptides after their digestion with elastase[14].

The hæmoglobin A peptides A-3 and A-9 differ only in that A-9 has an additional N-terminal lysine residue; we may write A-9 = Lys(A-3). The Lys-(A-3) bond in such a peptide would be attacked by trypsin only slowly; hence yields of peptides A-9 and A-3 were found to be variable.

(1) In D. K. P.'s hæmoglobin G, an asparagine residue in peptide A-3 (and A-9) has been replaced by lysine; hence a new trypsin-sensitive bond has appeared which results in the appearance of an additional tryptic peptide. Therefore we can write:

$$\text{A-3} \rightarrow \text{G-3}a + \text{G-3}b$$
$$\text{A-9} \rightarrow \text{G-9}a + \text{G-3}b(= \text{G-9}b).$$

Of course, peptide G-9*a* = Lys-(G-3*a*), as illustrated in Fig. 3.

(2) It so happens that peptide G-3*b* contains methionine, which in the course of fingerprinting is

Fig. 1. Starch-gel electrophoresis of D. K. P.'s hæmoglobin at *p*H 8·6 in 0·05 *M* veronal buffer

to some extent oxidized to the sulphoxide. The resultant peptide 'G-3*b* ox' is definitely identifiable, since it is separated in chromatography. Peptides A-3 and A-9 (and for that matter A-25) show the same oxidation phenomenon.

Hæmoglobin X was also digested and fingerprinted[11]. It is clear from the results (Figs. 2 and 3) that hæmoglobin X contains the abnormal peptides characteristic of both hæmoglobin C and G. Peptide A-4 (β chain) is replaced by the two hæmoglobin C peptides C-4*a* and C-4*b*. Peptides A-3 and A-9 (α chain) are replaced by the three hæmoglobin G peptides G-3*a*, G-9*a* and G-3*b*. Hæmoglobin X is therefore a naturally occurring adult hæmoglobin which is abnormal in both its α and its β chains. Such doubly abnormal hæmoglobins have been prepared *in vitro* by Itano and Robinson[12] using dissociation and re-association of suitable mixtures of singly abnormal human hæmoglobins.

One can now write the constitution of D. K. P.'s four hæmoglobins as follows:

$$\text{Hæmoglobin A} = \alpha_2^A\beta_2^A$$

$$\text{Hæmoglobin G} = \alpha_2^G\beta_2^A$$

$$\text{Hæmoglobin C} = \alpha_2^A\beta_2^C$$

$$\text{Hæmoglobin X} = \alpha_2^G\beta_2^C$$

We would deduce from these findings that D. K. P.'s genotype is $\alpha^A/\alpha^G\ \beta^C/\beta^A$ (see also in refs. 16 and 17). It has also been suggested before by Atwater *et al.*[5] that D. K. P. is doubly heterozygous for the G and C abnormalities. Apparently, each gene causes the manufacture of the peptide chain characteristic of it; thus, the α^A gene produces α^A chains, the α^G gene produces α^G chains with lysine in place of asparagine in peptide A-3, and so on. We must next assume that each chain dimerizes as soon as it is formed; $2\alpha^A \rightarrow \alpha_2^A$ and $2\alpha^G \rightarrow \alpha_2^G$. This must be so, since no real hybrids, such as $\alpha^A\alpha^G\beta_2^A$, etc., are produced, although all these chains are present inside the same cells. Finally, the four types of subunit seem to assemble to complete molecules in a random fashion, leading to the four hæmoglobins:

$$\alpha_2^A + \alpha_2^G + \beta_2^A + \beta_2^C \rightarrow$$
$$\alpha_2^A\beta_2^A + \alpha_2^G\beta_2^A +$$
$$\alpha_2^A\beta_2^C + A_2^G\beta_2^C.$$

It is important to realize the random nature of this final step in the assembly of the molecule, in contrast to the previous dimerization step, which is specific. The fact that the four hæmoglobins occur in roughly equal amounts, with A predominating, implies that at least in this patient the rate of manufacture of the different chains is only slightly different. As in the other abnormal human hæmoglobins, the phenotype corresponding to each gene is expressed and the product of all of them is to be found within the same cell.

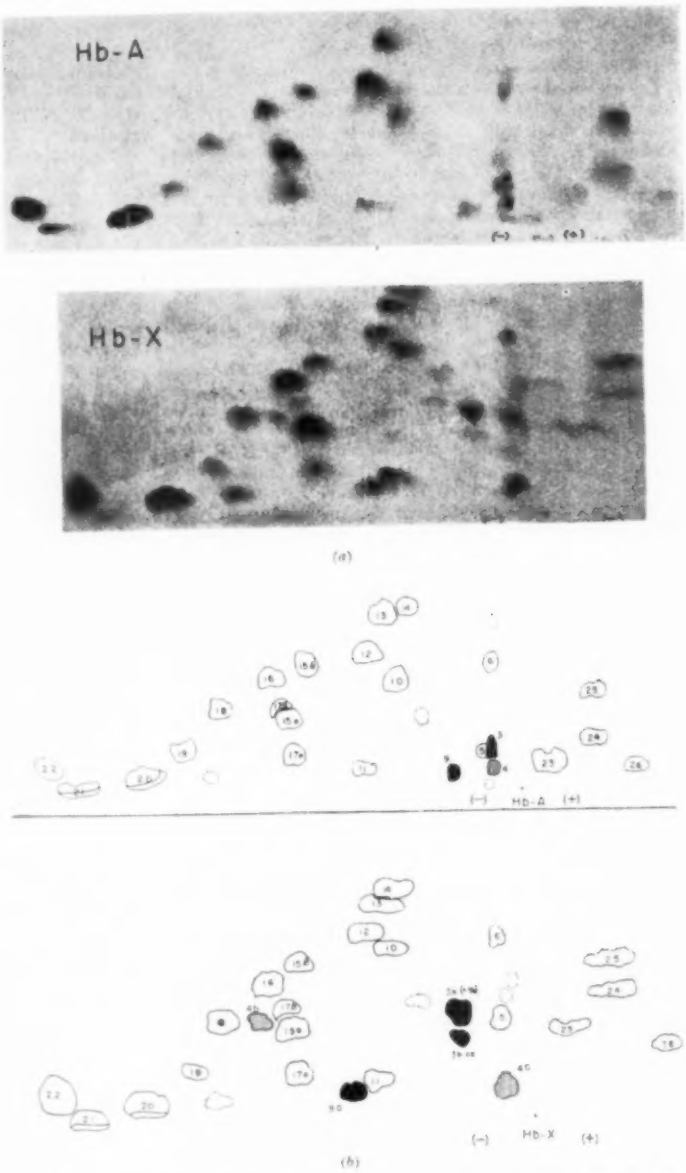

Fig. 2. Photographs (*a*) and tracings (*b*) of fingerprints (ref. 11) of hæmoglobins A and X. Electrophoresis was in the usual buffer but on a cooled brass plate at about 30 V./cm. for 2½ hr. Ascending chromatography in pyridine : isoamyl alcohol : water—35 : 35 : 30 by volume (ref. 18). The methionine residue in G-3*b* is often partially oxidized to the corresponding sulphoxide peptide with a different chromatographic mobility. Such an oxidized peptide is referred to as 'G-3*b* ox'. Peptides A-4, C-4*a* and C-4*b* are marked by a vertical shading. Peptides A-3, G-3*b*, G-3*b* ox and G-9*a* are marked in black

Rather similar chemical results are being obtained by Dr. Park Gerald, Boston, working with an apparently unrelated patient who possesses four haemoglobins called at present A, D, C and X. However, the four components are not nearly in equal amounts, haemoglobins C and X greatly predominating. It will be interesting to see whether these haemoglobins D and X are identical chemically with D. K. P.'s haemoglobins G and X and why the proportions are so different. Very recently, Raper *et al.*[20] reported briefly on the occurrence of A, G, C, X in one patient, with X abnormal in both chains. The relationship between their haemoglobins and ours remains to be determined.

Full details of our experiments have been submitted for publication.

We wish to thank Miss Jean Atwater and Dr. L. M. Tocantins for their help and interest. We would also like to acknowledge the help of Miss Marianne Schick, who performed the quantitative amino-acid analyses. This work has been supported by a grant from the Institute for Arthritis and Metabolic Diseases, U.S. Public Health Service.

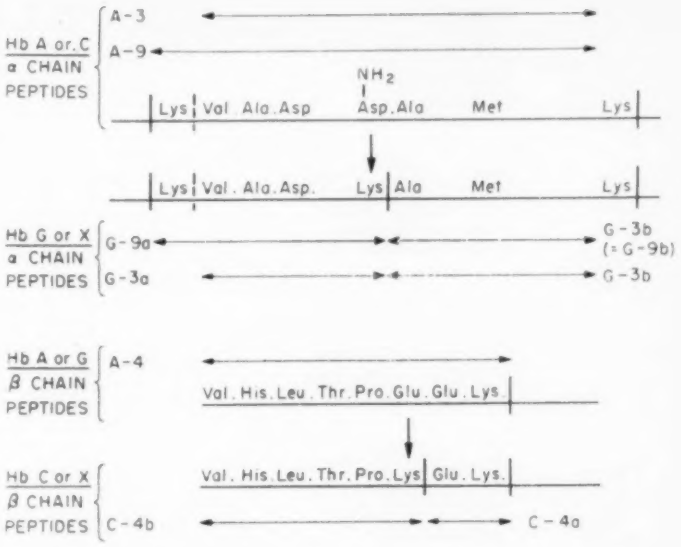

Fig. 3. Diagrammatic representation of the peptides obtained by the action of trypsin on the α- or β-chains of haemoglobins A, G, C, X. See text for the explanation of the relationship between peptide A-3 and A-9 and between G-3*a* and G-9*a*. In the lower part of the figure it can be seen that peptides A-4 and C-4*b* are at the N-terminus of the β-chains (ref. 19) of haemoglobins A and C. Peptide A-9 contains 29 amino-acid residues, peptide G-9*a* has 8

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GENETIC CONTROL OF FŒTAL AND ADULT HUMAN HÆMOGLOBIN

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ADULT human haemoglobin (A) is known to consist of two types of polypeptide chain of roughly equal lengths[1]. The gross formula of this haemoglobin may therefore be written as $\alpha_2\beta_2$, or more specifically as $\alpha_2{}^A\beta_2{}^A$, to indicate that the chains have the amino-acid sequences characteristic of haemoglobin A. The synthesis of α and β chains is supposedly controlled by separate α and β genes[2]. Fœtal human haemoglobin (F), on the other hand, has the constitution $\alpha_2{}^A\gamma_2{}^F$, indicating that this haemoglobin differs in the structure of only two of its four peptide chains[3]. Since Hunt[4] has shown that the α chains of fœtal and adult haemoglobin are similar, and probably identical, it became of interest to find out whether their production is controlled by the same α chain gene operating in the fœtus and in the adult. The investigations described in this article support the idea of control by the same α chain gene.

Haemoglobin I was first described by Rucknagel *et al.*[5] as an electrophoretically fast abnormal haemoglobin. An unrelated case of haemoglobin I, abnormal in the α chain[6], has more recently been found in a coloured woman, J. W., by Schwartz *et al.*[7]. J. W. is unusual in possessing 70 per cent haemoglobin I and 30 per cent haemoglobin A, whereas usually the

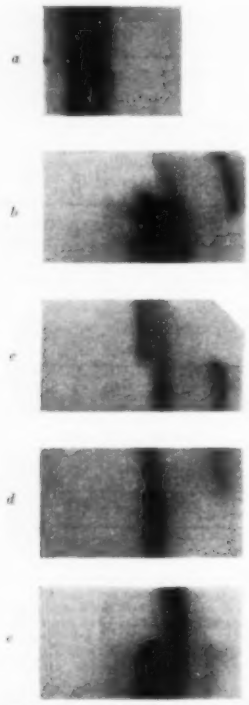

Fig. 1. Starch-gel electrophoresis (ref. 10) experiments in 0·02 *M* veronal buffer, *p*H 8·6. *a*, P. W., cord blood (upper sample) and blood with authentic hæmoglobin Bart's (lower sample); *b*, P. W., 1 day sample (lower) and hæmoglobin A + I from his mother, J. W. Overloaded to show the presence of Bart's in P. W. Note unexplained slow component in P. W., which is not hæmoglobin A_2; *c*, P. W., 2 months sample (upper) and hæmoglobin A + I. Hæmoglobin Bart's has largely disappeared from P. W.; *d*, P. W., 6 months (lower), showing absence of Bart's and fœtal hæmoglobin and hæmoglobins A + I; *e*, P. W., 1 day sample (lower) and 6 months sample

abnormal hæmoglobin comprises less than 50 per cent of the total. Atwater *et al.*[8] suggested that the explanation for this fact lies in J. W. being heterozygous for hæmoglobin I and for thalassæmia. On the basis of a recently developed hypothesis for the occurrence of the thalassæmia[9], we would picture J. W.'s *genotype* as:

$$\frac{\alpha^{I}}{\alpha^{Th}}\ \frac{\beta^{A}}{\beta^{A}}$$

The gene α^{Th} would cause the production of an α chain carrying a type of amino-acid substitution not detectable by electrophoresis, but which nevertheless drastically reduces the rate of production of such chains. Hence would follow the relatively low amount of hæmoglobin 'A'—really $\alpha_2{}^{Th}\beta_2{}^{A}$—in the blood of J. W.

Through the courtesy of Dr. L. Tocantins and Miss J. Atwater, we have been able to examine the blood of J. W.'s recently born son, P. W. Examination of the cord blood, and of a specimen collected at 24 hr., by starch-gel electrophoresis[10] at *p*H 8·6 in 0·02 *M* veronal buffer showed the presence of a fast-moving hæmoglobin component, judged to be 10 per cent of the total, in addition to hæmoglobins A and F (Fig. 1). By this method of electrophoresis the fast component had the same mobility as hæmoglobin Bart's[11], a variant of fœtal hæmoglobin, but was considerably slower than J. W.'s hæmoglobin I. The same result was obtained by electrophoresis on a starch block[12] at *p*H 8·6 in 0·05 *M* veronal buffer. The fast component was isolated and dialysed against 0·04 *M* phosphate buffer *p*H 8·0. Its absorption spectrum was normal with peaks at 578, 543, 412 and about 355 mμ, but in the ultra-violet region there was a pronounced tryptophan peak at 291 mμ which is characteristic[13] of fœtal hæmoglobin (Fig. 2). Hæmoglobin Bart's is a fœtal hæmoglobin known[14] to have the constitution $\gamma_4{}^{F}$ and to occur in the presence of thalassæmia[11].

The identity of baby P. W.'s fast hæmoglobin component with hæmoglobin Bart's was further demonstrated by comparing the behaviour of P. W.'s blood with an authentic specimen of hæmoglobin Bart's during ion-exchange chromatography on the carboxyl exchange *CG*50 type II according to Huisman and Prins[15] (Fig. 3). After development of the chromatogram for 30 min., hæmoglobins A and F were clearly separated. Ahead of them moved a well-defined hæmoglobin band at the same speed in the case of P. W.'s blood and in a specimen of hæmoglobin Bart's. Under these conditions, the hæmoglobin I moves between hæmoglobins A and F.

Baby P. W.'s fast hæmoglobin component, isolated by starch-block electrophoresis, was digested with trypsin and fingerprinted[16] alongside hæmoglobins Bart's and F. The pattern of tryptic peptides obtained from hæmoglobin Bart's and P. W.'s fast component showed the virtual absence of peptides 20 (α chain) 18, 9, 13 and 16 (ref. 15). These are characteristic of the α chain of human hæmoglobin. Hence, the fingerprints also suggest that this fast hæmoglobin has the constitution $\gamma_4{}^{F}$.

Recently, it was found that a precipitate had appeared in P. W.'s 24-hr. sample which had been stored frozen for a few months. At the same time, the fast hæmoglobin component had disappeared from the supernatant, which contained only hæmoglobins A and F. Hæmoglobin Bart's as well as hæmoglobin H (ref. 17)—$\beta_4{}^{A}$—are known to precipitate very easily. The precipitate from P. W.'s cord blood was fingerprinted by an improved method

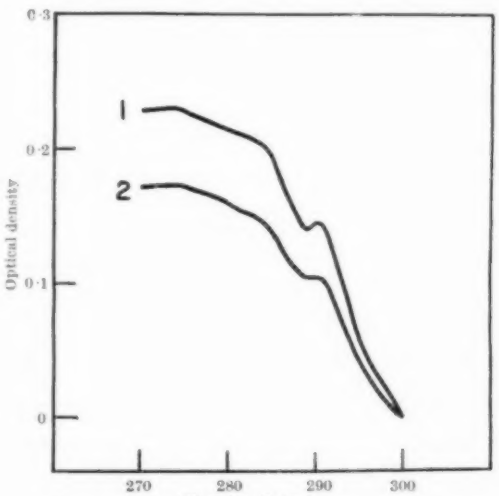

Fig. 2. Ultra-violet spectrum of P. W.'s fast hæmoglobin (1) and of hæmoglobin Bart's (2) isolated by starch-block electrophoresis (ref. 12)

(Fig. 4) and was seen to be largely composed of γ^F chains, as expected for hæmoglobin Bart's.

The fast component in P. W.'s blood had virtually disappeared at six months, as expected for a fœtal hæmoglobin[13].

These results indicated that baby P. W. possesses hæmoglobin Bart's —γ_4^F—but not the hæmoglobin I of his mother. As expected, baby P. W.'s hæmoglobin Bart's had disappeared by 6 months; but it was not replaced by the corresponding adult hæmoglobin H, which has the constitution β_4^A. Hæmoglobin H, like hæmoglobin Bart's, is usually associated with thalassæmia. Although one might expect *a priori* that the conditions which lead to hæmoglobin Bart's in the baby would also cause the appearance of hæmoglobin H in the adult, this is not necessarily so. Cases have been reported both in favour[18] and against[19] this expectation. The reasons for this variability are not clear.

Baby P. W. showed at 9 months a hypochromic microcytic blood picture[6]. It is reasonable to assume that baby P. W. inherited the α chain thalassæmia gene which is active in his mother, J. W., and which causes a decrease in the production of α peptide chains[2]. In turn, this situation would be expected to lead to an excess of γ chains, or rather γ_2^F dimers, which would then aggregate to form hæmoglobin Bart's. Baby P. W.'s genotype would be:

$$\frac{\alpha^{Th}\ \beta^A}{\alpha^A\ \beta^A}$$

The idea that the same α chain is concerned in the production of the adult and the fœtal hæmoglobin is an important one, since it allows us to formulate more clearly the probable mechanism involved in the switch from fœtal to adult protein. It is likely[20] though not undisputed that at the time of birth both hæmoglobins are present within the same cell. In that event, and in view of the findings reported above, we picture the change-over mechanism as involving the switching down of the activity of the γ chain gene and the switching on of the β chain gene, while the α gene remains active all the time.

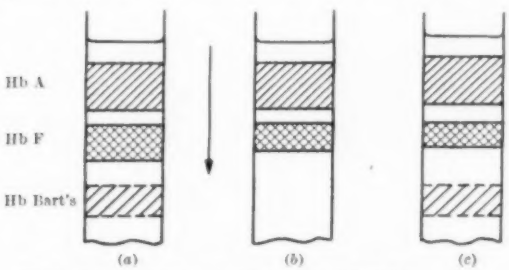

Fig. 3. Column chromatography (ref. 15) of P. W.'s hæmoglobin (*a*), of normal cord blood (*b*) and of blood with authentic hæmoglobin Bart's (*c*)

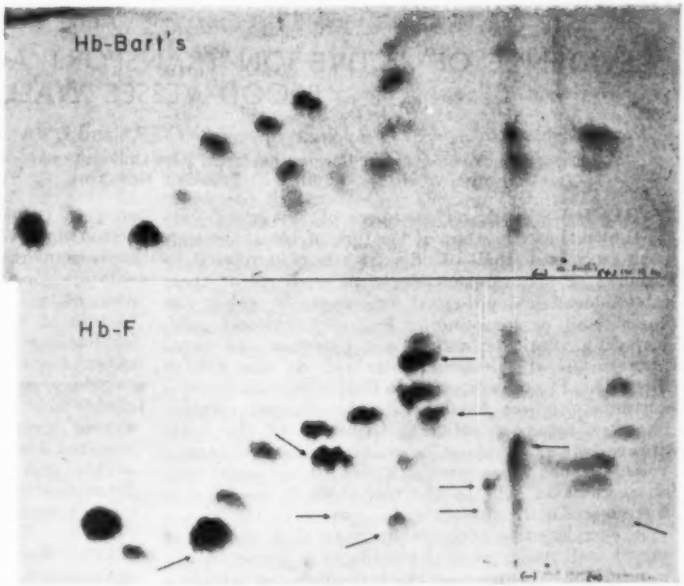

Fig. 4. Photograph of fingerprints (ref. 16) of precipitated hæmoglobin Bart's from baby P. W. and of hæmoglobin F. Electrophoresis was carried out at *p*H 6·4 on a water-cooled brass plate 24 in. long at 30 V./cm. for 2¼ hr. Chromatography was in pyridine : *iso*amyl alcohol : water—35 : 35 : 30 by volume (Wittmann, H. G., personal communication). α-Chain peptides of hæmoglobin F, as indicated by arrows, are largely absent in P. W.'s hæmoglobin Bart's

We wish to thank Dr. L. M. Tocantins and Miss Jean Atwater, Philadelphia, for their encouragement and for their generous help which made this investigation possible. Dr. H. Lehmann, London, generously supplied a sample of hæmoglobin Bart's. We would also like to acknowledge the many stimulating discussions with Dr. Park Gerald, Boston. This work has been supported by grants from the National Science Foundation and from the Institute for Arthritis and Metabolic Diseases, U.S. Public Health Service.

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EVIDENCE OF ACTIVE ION TRANSPORT ACROSS LARGE CANINE BLOOD VESSEL WALLS

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PREVIOUS work by members of this group has shown that disorders of the flow of blood through both large and small blood vessels appear related to induced or spontaneous electrical currents or their related electrical potential differences in either the vessel wall or surrounding tissues[1-3]. Blood cells, including platelets and blood proteins, are cataphoretic in an electrophoretic cell at the *p*H of blood[4-6]. It appears possible that abnormal electric currents produce local positively charged electrophoretic areas or other disturbance of the ionic atmosphere at the blood–intimal interface of damaged vessels; that these positive areas attract negatively charged blood cells to the blood vessel, resulting in intravascular thrombosis[7,8].

A correlated hypothesis suggests that the blood vessel wall under normal conditions expends energy moving ions to maintain the intimal–blood interface potential close to zero in a stable equilibrium. The measured transmural potential difference *in vivo* and *in vitro* appears to be very close to zero[7,9]. Experiments were designed to determine whether evidence for active ion fluxes across the blood vessel wall could be demonstrated.

These investigations were carried out using ion tracer techniques for the study of ion fluxes across membranes evolved by Dr. Hans Ussing[9] and others. Flux cells were modified after Hogben's design[10]. Fresh canine thoracic aorta or vena cava was opened along the long axis and divided into four equal samples of membrane. The segments were placed between four diffusion cell pairs so that each segment of wall formed a membrane 1 cm.² bathed on each side with oxygenated Krebs serum saline substitute[11] at 37° C. Tracer amounts of radioactive isotopes, 1 μc. of sodium-22, or sodium-24, and 1 μc. of chloride-36, were added to the intimal side in two of the cells and to the adventitial side in the remaining two cells to measure the rate of sodium, or chloride flux across the membranized blood vessel wall. One-ml. aliquots of the hourly removed recipient solutions were pipetted, dried and counted in a Geiger–Müller gas-flow counter. Flux was calculated in μmol./cm.²/hr. In selected experiments simultaneous trans-membrane potential differences were determined and compared with the measured ion fluxes across the blood vessel wall *in vitro*.

Ion flux determinations have been made on: (1) fresh, intact aortic wall; (2) aortic wall removed and stored for one or two days in Krebs serum saline substitute at 4° C.; (3) partitioned aortic wall, (*a*) the intima and subintimal layers in one cell compared with the (*b*) media and adventitial layers of the same segment of wall in a separate matching cell; (4) fresh vena cava wall. Only four of many groups studied will be dealt with in this communication.

Attempts were first directed at describing certain physical chemical characteristics of the blood vessel wall. Several groups of experiments resulted. These are: (1) Determination of the cumulative sodium flux across blood vessel wall for periods up to 6 hr. (2) The measurement of net hourly fluxes of sodium and chloride ions across aortic and vena caval wall to measure net ion transport (Fig. 1). (3) Determination of the oxygen dependency of the ion flux mechanisms in various experimental situations. These experiments fall into two groups. In the first group, matching pairs of aortic segments were exposed to aerobic and anaerobic conditions (Table 1). In the second group of experiments segments of membranized aortic wall were exposed to sequential 2-hr. aerobic and anaerobic periods (Fig. 2). (4) The determination of the temperature dependency of ion flux-rates.

Aorta. Dominant ion fluxes for both sodium and chloride occur from intima to adventitia across fresh, oxygenated, intact aortic wall membrane *in vitro* at a measured transmural potential difference very close to zero (approximate range, 0·3–2 mV.).

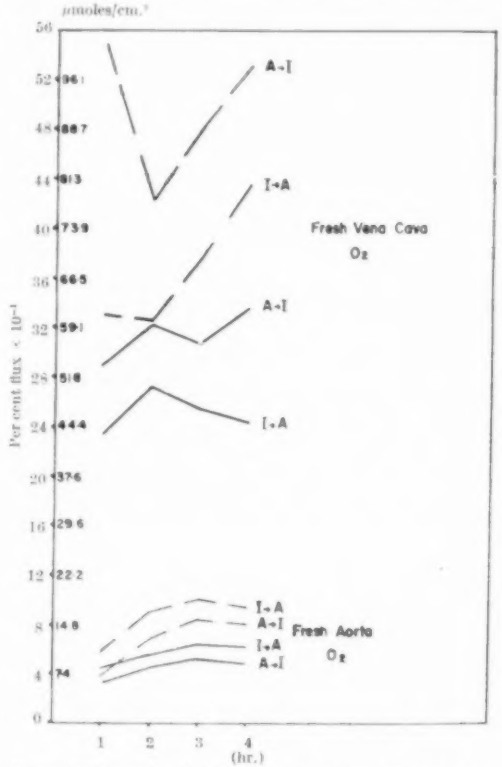

Fig. 1. Difference in rate of ion flux for membranized aortic and vena caval wall. Vena caval flux-rate is 4–5 times aortic flux-rate. *A→I* indicates flux from adventitia to intima; *I→A*, the reverse; O_2 indicates aerobic conditions. Chloride flux appears dominant for both vena cava and aorta. Vena cava dominant flux *A→I*; aortic dominant flux *I→A*
– – –, chloride-36; ——, sodium-24

* Markle Scholar in Medical Science.

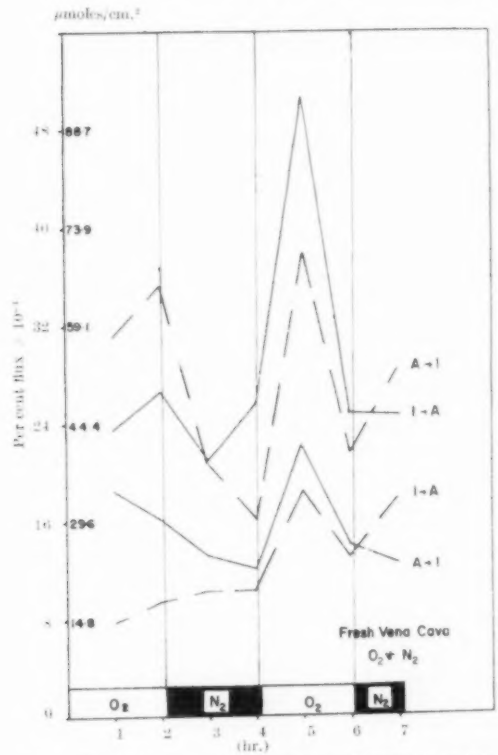

Fig. 2. The effect of consecutive ærobic and anærobic periods on sodium and chloride flux across vena caval wall. Under anærobic conditions sodium flux, $A \rightarrow I$, becomes dominant to chloride flux $I \rightarrow A$ in this experiment. The evidence indicates that sodium and chloride flux across vena caval wall is partially oxygen dependent, as shown for aortic wall in Table 1. ——, chloride-36; ——, sodium-24

Vena cava. Sodium and chloride flux-levels for vena cava are five to six times those for the aorta (Fig. 1). This fact can be explained only in part by the greater thickness of the aortic wall. Both sodium and chloride show a mean net parallel flux. Note, however, that net flux across the aorta occurs in the opposite direction to that across the vena cava.

Ærobic versus anærobic ion transport (*Fig.* 2). In matched experiments in which two samples of membrane were exposed to oxygen and two samples of membrane to nitrogen, net ærobic sodium flux was usually opposite in direction to net anærobic sodium flux. The absolute magnitude of net fluxes was always different in the two groups, being greater under ærobic conditions (Table 1). Sodium and chloride ion fluxes across both aorta and vena cava show at least two types of marked change during sequential ærobic and anærobic periods. An absolute change in flux-rate occurs on switching from ærobic to anærobic conditions. Sodium frequently replaces chloride as the dominant ion transported across vena caval wall on establishment of anærobic conditions (Fig. 2).

Temperature effects. The information from experiments in which cell temperature was raised in steps indicates that the ion flux increases approximately 8–15 per cent per deg. C. rise from 8° to 56° C. The rate of flux increase per deg. C. closely parallels the changing rate of metabolic activity one might expect if sodium and chloride flux occurred across the blood vessel wall as the result of a metabolic process.

An Arrenhius plot of the rates of sodium and chloride ion flux indicates that the absolute rate of flux per deg. C. change varies critically at approximately 25° C. and again at 40° C. (Fig. 3).

Under the conditions of the experiment described, the greater part of ion movement across the blood vessel wall appears to be passive. Proof that all the ion movement is not passive is indicated by evidence presented in this article.

(1) Sodium and chloride fluxes across the membranized blood vessel wall are not identical in each direction.

(2) Net sodium and chloride ion movement across the aortic wall appears to be oxygen-dependent; net flux frequently reverses onestablishment of anærobic conditions. The flux-rate change per deg. C. change in the temperature experiments and correlated Arrhenius plots also indicates active transport. By definition, both chloride and sodium flux in these

Table 1. SODIUM-22 FLUX ACROSS AORTIC WALL
Matched pairs of ærobic and anærobic determinations

Exp.	Gas	Direction of dominant flux		Non-heparinized Mean hourly flux μM/cm.²/hr.		Net flux direction	N_2–O_2	Comments
		$A \rightarrow I$	$I \rightarrow A$	$A \rightarrow I$	$I \rightarrow A$	$(A \rightarrow I) - (I \rightarrow A)$		
64	N_2	X		14·78	10·2	+ 4·58	+ 4·27	Fresh
65	O_2		X	12·65	12·34	+ 0·31		
66	N_2	X		12·52	11·22	+ 1·30	+ 4·75	Aorta stored 1 day at 4° C.
67	O_2		X	11·46	14·81	− 3·45		
68	N_2	X		10·7	8·1	+ 2·60	+ 3·02	Fresh
69	O_2		X	11·23	11·65	− 0·42		
70	N_2		X	13·37	14·72	− 1·45	+ 1·20	Aorta stored 1 day at 4° C.
71	O_2	X		8·85	11·5	− 2·65		
78	N_2		X	14·7	11·6	+ 3·1	+ 4·70	Fresh
79	O_2			13·1	14·7	− 1·6		
				New series				
345	N_2	X		10·46	8·06	+ 2·40	+ 0·51	Fresh
344	O_2	X		8·44	6·55	+ 1·89		
347	N_2	X		12·42	6·83	+ 5·59	+ 6·71	Fresh
346	O_2		X	7·77	8·89	− 1·12		
349	N_2	X		16·89	11·90	+ 5·99	+ 8·45	Fresh
348	O_2		X	9·22	11·68	− 2·46		
							* t = 4·494 P = 0·001	

* t = Results of 't' test for statistical validity of results. P = Possibility that result is due to chance, in per cent.
Data from eight matched pairs of ærobic and anærobic experiments measuring sodium flux across the aortic wall. Both direction and rate of sodium flux vary under the contrasted conditions ($P < 0{\cdot}001$).

Table 2. CALCULATED AND MEASURED POTENTIAL DIFFERENCES AS DETERMINED BY THE STANDARD DONNAN EQUILIBRIUM EQUATION

	Na-22, Na-24 experiments				Cl-36 experiments			
	f_i/f_o mean	Calculated *PD*	Measured *PD*	No. of flux exps.	f_i/f_o mean	Calculated *PD*	Measured *PD*	No. of flux exps.
Aorta	0·9193	+ 4·25 mV.	≈ 1·0 mV.	29	0·9726	+ 1·31 mV.	≈ 1·0 mV.	13
Vena cava	1·5634	− 10·11 mV.	≈ 1·0 mV.	13	1·5836	− 9·88 mV.	≈ 1·0 mV.	14

f_i = inward flux, adventitia to intima.
f_o = outward flux, intima to adventitia.

experiments appear to be active transport, since the blood vessel wall or some of its layers bathed with identical solutions on each side move ions differentially at a measured potential difference close to zero. The results for the experiment for sodium and chloride flux exceed by 5–10 times the fluxes necessary to satisfy Donnan equilibrium equations at 37° C. (Table 2). For any univalent ion :

$$\frac{f_i}{f_o} = \frac{C_i}{C_o Z}$$

$$C_i = C_o$$

$$\frac{f_o}{f_i} = Z$$

$$Z = \exp(Ef/RT)$$

$$Z_{37°C.} = 10^{PD/0·61}$$

$$PD = 61 \log Z_{37°C.}$$

where E is potential difference (PD) in mV., f is Faraday's constant, R is gas constant, T is absolute temperature, if ion movement across the membrane is passive.

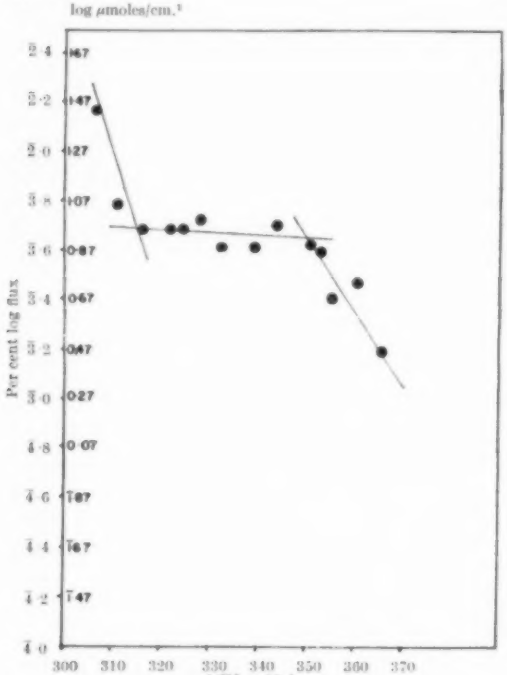

Fig. 3. An Arrhenius plot of sodium-24 flux-rate $I \rightarrow A$ across vena caval wall during which cell temperature was raised from 8° to 65° C. Log per cent flux is plotted to the left of abscissa, log μm./cm.²/hr. to the right. The reciprocal of the absolute temperature is plotted on the ordinate
The results indicate that absolute change in flux-rate occurs as certain temperature-levels are reached

Net transport of one ion may occur at a very small transmural potential difference (1–2 mV.) under the conditions of this experiment only if equal amounts of another ion of equal and opposite sign accompany the measured ion across the experimental membrane, or an ion or ions of like or equal charge move in opposite direction across the membrane. Which of the two already-mentioned possibilities pertain to the situation described has still to be ascertained, for several other ions available to the vessel wall membrane could easily be transported during these experiments.

Do these experiments, performed *in vitro*, mirror phenomena which occur in living blood vessels *in vivo*? Evidence is available which indicates that brain capillaries do not fulfil Donnan equilibrium requirements and show evidence of active transport *in vivo*[12]. Whether the experiments described in this article relate to similar phenomena across smaller blood vessels and capillary walls has still to be determined.

Much has been conjectured concerning the fact that aortic and vena caval wall transport in opposite directions. Experiments and theory attempting to explain the difference will be offered in later publications.

Close to the blood intimal interface the net charge due to small net positive or negative ion transport across vessel walls may have a considerable though short-lived effect on interface potential differences. It would appear that tissue injury currents could derange this type of ion transport mechanism if of sufficient magnitude, and might result in reversal of net ion transport as is shown frequently in anærobic experiments in this work. It is conceivable that vascular occlusion due to spontaneous tissue injury or due to applied small pseudo-injury currents might occur as a result of derangements in the flux mechanisms described here.

We wish to acknowledge the aid given by Dr. Adrian Hogben and Dr. Kenneth C. Cole in the course of these experiments.

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LETTERS TO THE EDITORS

GEOPHYSICS

Upper Limit for Interstellar Millicycle Gravitational Radiation

THE effect of gravitational radiation on an elastic body has been previously investigated[1]. The component varying with time of the Riemann tensor (R_{iojo}) associated with the gravitational field acts as a driving term in the wave equation for the strain or displacement. It was proposed[1] that the normal modes of the Earth or a laboratory mass be used as a detector of gravitational radiation. Experiments to measure the interstellar gravitational radiation at kilocycle frequencies are at present in progress at the University of Maryland.

From theoretical arguments we expect the interstellar gravitational radiation noise spectrum to show a peak at very low frequencies. It would therefore be advantageous to use a detector with as low a frequency response as possible. The largest mass available for an experiment is the Earth itself. The various theoretical modes for the vibration of the Earth have been known since 1882. However, it has not been until recently[2] that instruments with sufficiently long period have been available to measure the frequency and amplitude of these modes.

The data used were obtained from the N.32° W. Benioff strain seismograph at Isabella, California. The amplitude of the strain in the Earth's crust has been analysed from these data at the Seismological Laboratory of the California Institute of Technology, with the aid of the computational facilities at the Sandia Corporation[2]. Measurements taken after the recent Chilean earthquake were sufficient to identify the various vibrational modes and determine their breadth and frequency.

The data taken from the Isabella strain gauge during a quiet period do not show peaks at the frequencies of the various vibrational modes, hence the strains observed by the gauge are extraneous strain noise above the level of the actual strains in the modes during a quiet period. The data are therefore only useful for setting an approximate upper limit for the effects of gravitational radiation. Because of this, an exact analysis of the effect of the Riemann tensor on the various vibrational modes, although possible, would be of little value. For the purpose of calculating an upper limit, we shall use the equations obtained by Weber for the magnitude of the strains induced by the Riemann tensor in a longitudinally vibrating rod[1].

The strain in the elastic body at resonance is related to the Riemann tensor by:

$$\varepsilon(\omega) \approx \frac{2c^2Q}{\omega^2\pi} R_{iojo}(\omega) \qquad (1)$$

Here $\varepsilon(\omega)$ and $R_{iojo}(\omega)$ are the Fourier transforms of the strain and Riemann tensor, respectively, ω is the angular frequency, c is the speed of light and Q is the ratio of the frequency to the resonance half-intensity width. By squaring equation (1) and integrating over all frequencies, we obtain for the mean squared strain associated with a given mode:

$$\overline{\varepsilon(t)^2} \approx \frac{4c^4Q}{\pi^2\omega^3} R^2_{iojo}(\omega) = \frac{60GQ}{c^3\omega} t_{or}(\omega) \qquad (2)$$

In equation (2), $R^2_{iojo}(\omega)$ is the power spectrum of the Riemann tensor, G is the constant of gravitation and $t_{or}(\omega)$ is the power spectrum of the incident gravitational energy flux, assuming the radiators are at rest relative to the Earth.

The results obtained by the Seismological Laboratory and the upper bound to the Riemann tensor and energy flux power spectra are given in Table 1 for a number of frequencies. The strain data were smoothed since the fluctuations observed were random and not correlated with the modes of the Earth.

Table 1

Fundamental mode	Period (min.)	Q (est.)	Strain² (av.)	$R^2_{iojo}(\omega)$ $\left[\frac{1}{\text{cm.}^4\ \text{(rad./sec.)}}\right]$	$t_{or}(\omega)$ $\left[\frac{\text{watts}}{\text{cm.}^2\ \text{(rad./sec.)}}\right]$
S_3	54·0	400	80×10^{-16}	$< 0{\cdot}5 \times 10^{-75}$	< 20
S_4	25·8	350	20	2	20
S_6	16·0	300	8	3	10
S_8	11·81	250	4	5	10
S_{10}	9·66	210	2·5	7	10
S_{14}	7·47	180	1·2	10	10
S_{20}	5·78	160	1	20	10
S_{30}	4·37	120	0·6	30	10
S_{38}	3·66	100	0·6	60	10

This table indicates that the Riemann tensor power spectrum of the incident gravitational radiation cannot be larger than $\approx 10^{-75}$/cm.⁴ (rad./sec.) in the vicinity of 1 c./hr. The figures for the energy flux are very high [20 watts/cm.² (rad./sec.)], but not particularly meaningful. The energy associated with a given Riemann tensor depends on the reference frame in which it is defined. We chose the rest frame of the assumed radiator. If we had calculated in a rest frame fixed in the Earth's centre of mass, and averaged over the volume of the Earth, numbers for the energy flux about ten orders less would have been obtained. This is because the Earth is in free fall and the energy flux always vanishes at the pole of a geodesic co-ordinate system. Another assumption is that the Earth is behaving like an elastic body when driven by the Riemann tensor. If the Earth behaved like a liquid, the surface strains would be several orders less for a given Riemann tensor and the limits of the table correspondingly greater.

Earth strain data enable calculation only of the power spectrum of the Riemann tensor. Other effects, such as the fluctuation of the Earth's rotation period, enable the total flux to be estimated[1].

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A Maximum of Temperature in the Middle Ionosphere

J. Fuchs[1] has already pointed out the fact that from the change of electron-density (N) with height (h) conclusions as to the temperature in the ionosphere can be drawn. It was, however, not possible then to carry out exact calculations for two reasons: first, the electron-density was only known to be dependent on the apparent height (h'), and secondly, the process of electron loss was not known in more detail, so that Fuchs had to calculate with a recombination-coefficient constant as to space and time.

To-day these two difficulties have been overcome: some institutions have for some time been publishing detailed $N(h)$ profiles, for example, the Central Radio Propagation Laboratory (Boulder) hourly values for the station Puerto Rico. For the process of electron loss, I[2] have introduced the following equation:

$$L = \alpha_0 p^k . T^n . N^{m=2}$$

It has been possible recently to define the constants k and n and this has enabled me to determine from the $N(h)$ profiles the height dependency of scale height (H) and density. The results with regard to the observations of Puerto Rico can be summarized as follows:

(1) The scale height has during the day a maximum at a height of about 200 km. (2) The value of this maximum shows a considerably daily and yearly variation. In the early morning and late afternoon the maximum is much less noticeable than at noon. (3) The height in which this maximum occurs shows a corresponding daily and annual variation: at noon during the summer the maximum of H rests at a height of about 220 km.; it descends to about 180 km. in the morning in winter. (4) Above this maximum the scale height decreases rapidly, and I presume that the gradient dH/dh is getting small only a little below the $F2$ peak. (5) The decrease in density with height corresponds roughly to the result which Priester[3] was able to publish recently.

This research is sponsored by the European Research Office (Contract No. 3983-S).

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GEOLOGY

Flow Folding in Rocks

Prof. L. U. de Sitter[1] considers that in flow folding "internal movement itself is no longer orientated but can take any direction", and that the position of shear planes is random. He believes it developed most typically in incompetent rocks like salt, or at very high confining pressures or high temperatures. It is further maintained that this is the only true plastic deformation of rocks. These beliefs have recently been reiterated and enlarged on[2].

Such views appear to be becoming general, and Ball[3] further characterizes monogenetic folds formed by flow by stating that "the quartz fabric will tend to be markedly heterogeneous, and the symmetry of the fabric will not correspond to the symmetry of the fold".

A brief account of the concepts on plastic flow of rocks will indicate that the current use of the term 'flow' has probably to do with only one type, which is difficult to accept as occurring within rocks.

Flow in rocks is a permanent change of form without apparent rupture, and any fracturing that may occur is microscopic. This property of flow is referred to as plasticity[4]. Above microscopic level such plastic flow is a continuous deformation where neighbouring points in the material remain so during the deformation.

Leith[5] and others have stated that flow takes place by interior readjustments of rock substances by chemical, mineralogical, and mechanical changes. Commonly, the deformation results in a parallel arrangement of the constituents of the rock mass, producing a banded structure, schistosity or cleavage[6]. However, flow may leave no evidence in any parallel arrangement.

Little is known of the mechanics of plastic flow. Nevertheless, possible comparisons between plastic and viscous flow can be made[7], and the mechanics and the successful application of steady, stable, laminar flow to a number of folds have been described in papers by Cloos[8] and Carey[9,10].

Folds that appear to have resulted from a laminar type of flow more or less perpendicular to the rock layers are characterized by thickened and thinned beds, crenulation of bedding planes, and generally a persistence in depth. Where planar discontinuities have developed and folding has progressed by movement along these planes the resulting deformation has been termed a shear fold.

It appears that these laminar-flow folds are excluded from de Sitter's class of flow folds which, because of the postulated random movement, must refer to a mechanism comparable with turbulent viscous flow.

According to reasonable calculations magma is intruded in most dykes by means of laminar flow and turbulence is only achieved in those magmas which have low viscosity due to super-heating or to a high content of volatile material[11]. By analogy it appears most unlikely that a type of turbulent flow can ever be achieved within rocks, which have, in comparison, enormously high viscosities.

It is, therefore, suggested that the folds at present believed to belong to de Sitter's class of flow folds should be reconsidered, and attempts made to interpret them in terms of laminar flow, for not all folds that result from laminar flow may appear geometrically simple. It has been proposed that lateral laminar flow along involuted planes within liquefied layers of sand can account for convolute folding that may occur within them[12]. Is it perhaps possible that the complicated plastic folds with, at first sight, random orientation of the foliations, are in point of fact due to similar unusual patterns of laminar flow?

It appears that the class of flow folds, the present status of which is here questioned, should be redefined to include folds resulting from laminar plastic flow. In so far as all rocks flow during folding, limits must necessarily be rather arbitrary. Competent layers, which retain approximately their original thickness perpendicular to the bedding, show only sufficient flow for them to be flexed. Thus, flexural or concentric folds, and folds of patterns determined by the flexing of competent layers within an interbedded sequence of competent and incompetent horizons would be omitted. Only those folds determined by flow rather than flexure should be included. Flow

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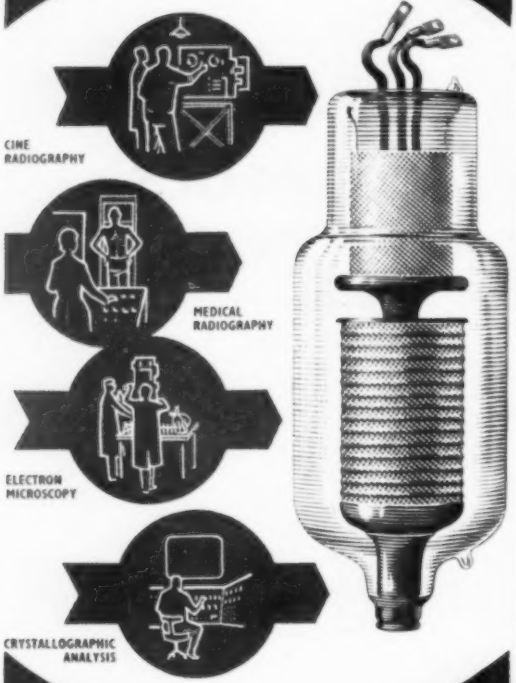

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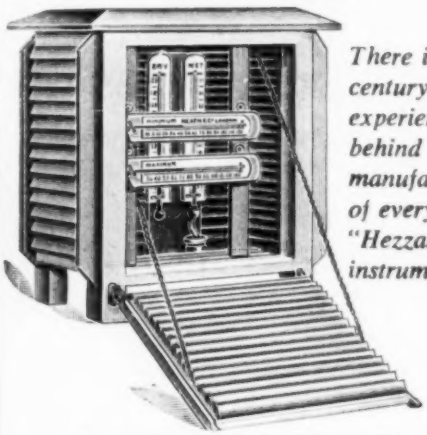

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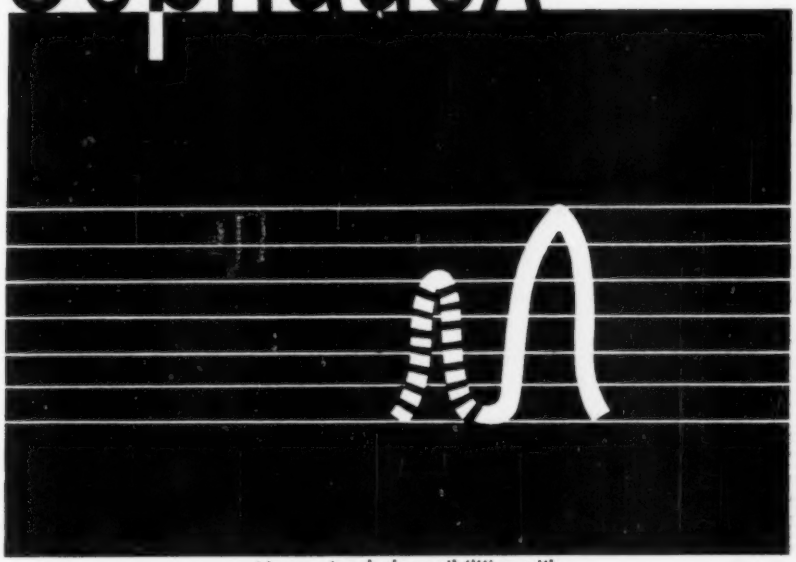

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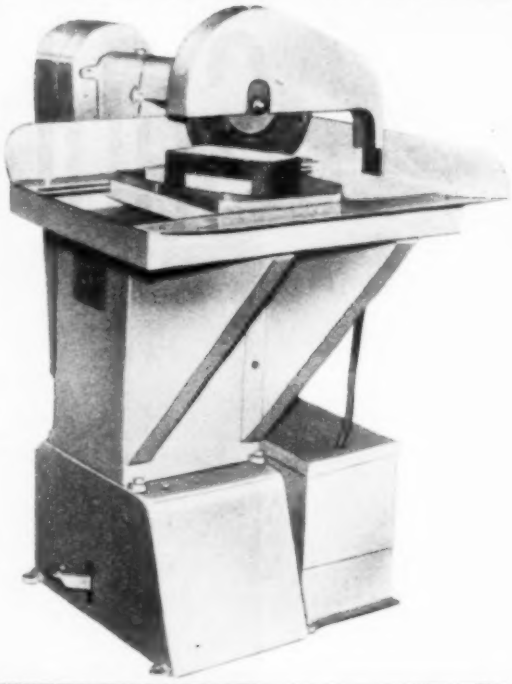

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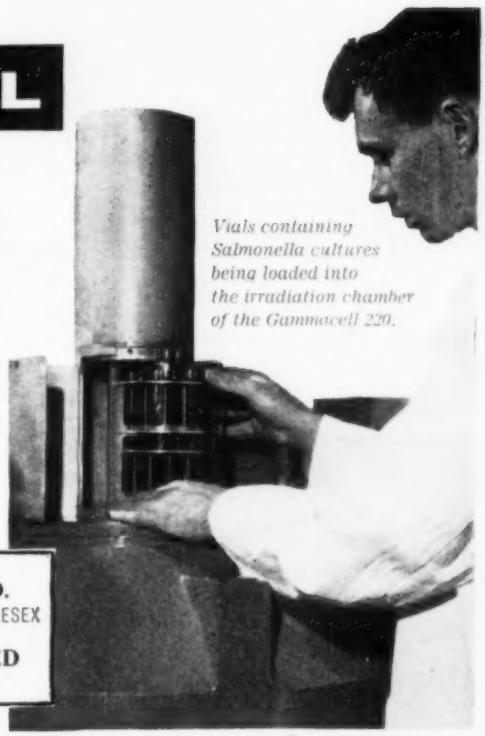

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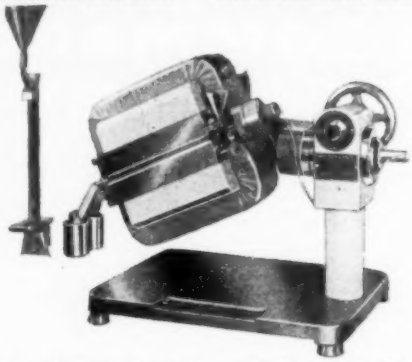

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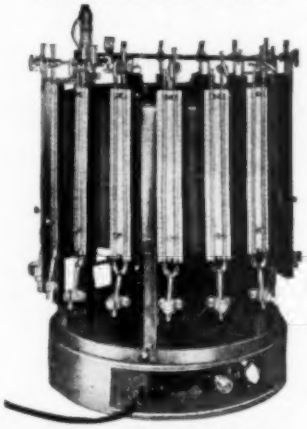

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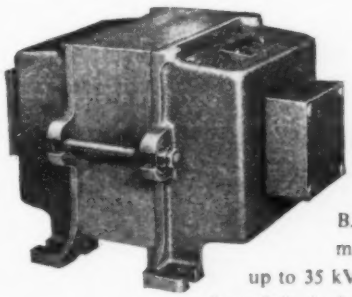

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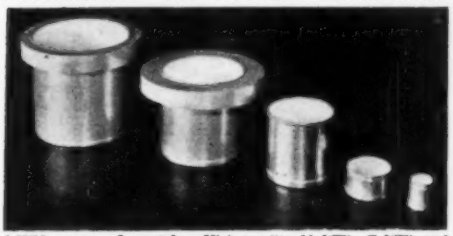

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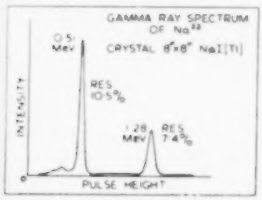

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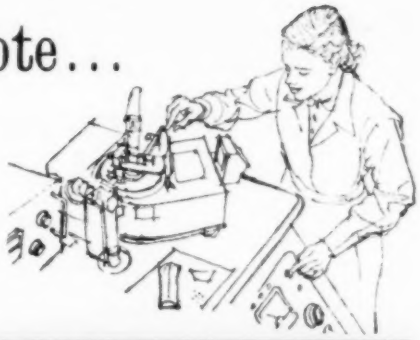

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folds may, therefore, be defined as contortions affecting only incompetent beds, which have thickened and thinned without the aid of ruptures above microscopic levels.

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EMYR WILLIAMS

Geological Survey Department,
P.O. Box 789,
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Basutoland Kimberlites

SINCE 1954 a prospecting programme for diamonds in the British Protectorate of Basutoland has led to the discovery of a new predominantly basaltic kimberlite province to the east of the micaceous kimberlite province in the Orange Free State of the Union of South Africa. The kimberlites are intruded into Karroo sediments and lavas and comprise both dykes and diatremes. Petrographically the kimberlites are similar to kimberlites in other parts of South Africa[1,2] and they contain inclusions of eclogite, granulite, peridotite and ilmenite in addition to inclusions of the Karroo country rocks.

Spectrographic analyses of the kimberlites reveal that the trace elements, like the major elements, can be divided into two contrasting suites: (*a*) those in amounts typical of ultrabasic rocks; (*b*) those in amounts typical of alkaline late differentiates. Like the ultrabasic potassic rocks of Uganda which exhibit similar chemical features[3,4], it is believed that kimberlite owes its origin to reaction between a carbonatitic magma and crustal granite. More detailed results are to be published shortly.

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* Formerly of the Department of Geology, University of Leeds.

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PHYSICS

Normal Mode Interpretation of the Sound Propagation in Whispering Galleries

THE propagation of sound in 'whispering galleries'[1] is a very remarkable phenomenon, and in Lord Rayleigh's *Theory of Sound* he gives his well-known interpretation based on observations at St. Paul's Cathedral in London. According to my observation, which agrees with Lord Rayleigh's comment in his book, the opinion of the Astronomer Royal ascribing the phenomenon to the reflexion at the upper dome is hard to accept. This follows because at the diametrically opposite point of the gallery the whisper can scarcely be heard, whereas it becomes stronger as one approaches the speaker.

Lord Rayleigh's explanation is, to use present-day terminology of elastic surface waves, based on 'ray theory'. There is, however, another way of describing so-called 'normal mode theory', and the following analysis based on this theory is in accord with the ray theory interpretation given by Lord Rayleigh.

Adopting the velocity potential ϕ, we have a solution referred to polar co-ordinates R, θ and φ as follows:

$$\phi = ([p/c]R)^{-1/2} J_{n+1/2}([p/c]R) Y_n(\theta,\varphi)\exp(ipt) \quad (1)$$

where p is the frequency, c the velocity of sound, J_ν is the Bessel function and $Y_n(\theta,\varphi)$ the spherical surface harmonics. Assuming that the wall is approximately rigid, the boundary condition, a, being the radius of the gallery, is:

$$\text{at } R = a: \quad \partial\phi/\partial R = 0 \quad (2)$$

which gives an equation of the form:

$$\partial[\xi^{-1/2} J_{n+1/2}(\xi)]/\partial\xi = 0, \quad \xi = (p/c)a \quad (3)$$

Since the circumference of the gallery is roughly 100 yards, and the wave-length of the voice is about 1 yard, n is about 100.

Trying the numerical solution for smaller values of n, we find that $n + 1/2 < \xi$. Hence we employ the next form of asymptotic formula for the Bessel function with large orders[2]:

$$J_\nu(\nu\sec\beta) \sim \left(\frac{2}{\pi\nu\tan\beta}\right)^{1/2}\left[\cos Q + \frac{1}{\nu}\cot\beta\cdot\left(\frac{1}{8} + \frac{5}{24}\cot^2\beta\right)\sin Q\right] \quad (4)$$

$$Q = \nu(\tan\beta - \beta) - \pi/4$$

and put it into the above expression. Then we have the characteristic equation:

$$\frac{1}{\nu}\left(\frac{7}{24}\tau^3 + \frac{7}{8}\tau\right) + \left[\frac{1}{\nu^2}\left(\frac{35}{48}\tau^6 + \frac{35}{24}\tau^4 + \frac{9}{8}\tau^2\right) + 1\right]\cdot\tan Q = 0 \quad (5)$$

$$\tau = \cot\beta$$

$$\nu = n + 1/2 \text{ and } \nu\sec\beta = \xi \quad (6)$$

The approximate solution of this equation is obtained assuming that $\nu\beta^3$ tends to a certain value different from zero when ν increases indefinitely, namely:

$$\frac{7}{24}\frac{1}{\nu\beta^3} + \left(\frac{35}{48}\frac{1}{\nu^2\beta^6} + 1\right)\cdot\tan\left(\frac{1}{3}\nu\beta^3 - \frac{\pi}{4}\right) = 0 \quad (7)$$

The root is

$$\nu\beta^3 = 1{\cdot}99 \quad (8)$$

which, combined with (6), gives:

$$\xi = (n + 0{\cdot}5) + 0{\cdot}79(n + 0{\cdot}5)^{1/3} \quad (9)$$

The intensity distribution of ϕ with regard to radial direction is given by the function:

$$\Phi = A\cdot([R/a],\xi)^{-1/2} J_{n+1/2}([R/a],\xi) \quad (10)$$

in which n and ξ are connected by the relation (9). This function can be evaluated by the above asymptotic expansion (4) and other similar formulæ.

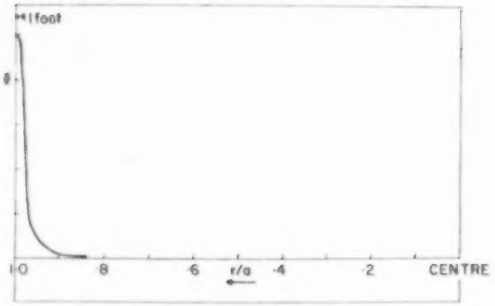

Fig. 1

Assuming $n = 100$, I carried out the numerical computation of the function Φ, in which A was given a value such that the function becomes unity at the surface $R = a$.

The property of the curve given in Fig. 1 agrees well with my auditory observation in St. Paul's Cathedral. If the ear is moved about 10 in. from the wall the intensity of the sound does not change much; but after that it falls off rapidly. Since the circular corridor along the wall is about 6 ft. wide, the observation cannot be continued further than that; but in fact the whisper is scarcely audible at the edge of the corridor.

These characteristics are exactly those of the so-called guided waves. In a homogeneous medium of half-space, sound waves do not give surface waves like Rayleigh waves in a solid. However, if the medium is surrounded by a rigid spherical wall, a kind of guided wave can exist, and this is what is observed in whispering galleries. The surrounding wall is neither exactly spherical nor circular cylindrical in the case of St. Paul's Cathedral; but these calculations give a rough approximation of what takes place in the gallery.

Yasuo Satô

Lamont Geological Observatory,
Columbia University,
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Measurement of Pressure in Vacuum Physics

The torr has recently been adopted as the British standard unit for the measurement of pressure in vacuum physics; but the fact that proposals have been made for further change[1,2] indicates that the present system is not yet satisfactory. The recent proposals have been concerned with definition of units; but the practical expression of pressures in terms of these units appears also to be due for revision.

The range of pressures encountered in vacuum physics is at present about 10^3–10^{-11} torr, so that to cover this range with a single unit the conventional method is to use the exponent; the alternative method of expression of pressures as small decimal fractions of a torr is obsolescent, and its main continued use appears to be in the usual calibration of the scale of the McLeod gauge. Thus we are at present expressing pressures less than atmospheric with a range of exponents which may be positive or negative, with the zero exponent corresponding to no clearly recognizable pressure. As improvements in high-vacuum techniques continually decrease the pressures attainable in vacuum systems the problem of expression becomes aggravated as we are forced to use larger negative exponents; this makes more obvious the terminological inconsistency of a 'higher' vacuum corresponding to a smaller number.

A similar problem, the expression of hydrogen-ion concentration in aqueous solution, was elegantly solved by the introduction of the *p*H scale, which has been universally adopted and has proved satisfactory over many years of use. In most vacuum measurements the problem is quite analogous; we are concerned mainly with the order of magnitude of the pressure.

It is proposed therefore that the new unit the vac[2], which has excellent theoretical justification, would be an ideal basis for a *p* Vac scale. If zero on the scale is taken as 10^3 vac, which is almost one standard atmosphere, it is possible to define a scale analogous to the *p*H scale:

$$p\ \text{Vac} = -\log \text{vac} + 3$$

Thus, zero is atmospheric pressure, all practical vacua will be positive, and the larger *p* Vac, the higher the vacuum.

W. W. Forrest

Division of Biochemistry and General Nutrition,
Commonwealth Scientific and Industrial
Research Organization,
University of Adelaide.

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The Special Theory of Electromagnetism

The law of addition of collinear velocities as derived from the Lorentz transformation in special relativity is:

$$W = \frac{U + V}{1 + UV/c^2} \qquad (1)$$

U and V being the components, W the resultant velocity and c the velocity of light. It follows that W can never be greater than c.

Despite this failure in kinematics of the classical law of vector addition, that law is still used in other fields of physics. This communication shows what modifications to electrostatic theory are necessary if a rule analogous to equation (1) is adopted in its place.

Introducing 'electric interval' $d\sigma$ by the relation:

$$d\sigma^2 = dr^2 - \varkappa^{-2} d\varphi^2 \qquad (2)$$

where dr and $d\varphi$ have their usual meaning for an observer and $\varkappa$ is a universal constant, the addition of collinear electric vectors now follows the rule:

$$E = \frac{E_1 + E_2}{1 + E_1 E_2/\varkappa^2} \qquad (3)$$

and $\varkappa$ is recognized as the limiting attainable resultant, presumably corresponding to a break-down field-strength.

Discrepancies from classical theory will be imperceptible in weak fields, so that support for the new hypothesis must be sought under conditions near breakdown.

Considering the inverse square law, a geometrical concept in which the possible effect of the field on measurement of distance is ignored, it appears that distance must be replaced by interval in its formulation, so that the field of an electron is represented by :

$$\frac{d\varphi}{d\sigma} = -\frac{e}{\sigma^2} \qquad (4)$$

e being the charge. The measured field-strength is then :

$$\frac{d\varphi}{dr} = -e(\sigma^2 + e^2/\chi^2)^{-1/2} \qquad (5)$$

which compares with the Born and Infeld formula.

B. L. Coleman

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CRYSTALLOGRAPHY

Out-of-Focus Electron Microscope Images of Edges of Crystal Lattices

In a recent communication, Hashimoto and Watanabe[1] report the observation of extra lines outside the geometric bounds of the electron microscope image of a crystal of copper phthalocyanine when the microscope is de-focused to obtain the Fourier image of order $N = \frac{1}{2}$ (see Cowley and Moodie[2]). They state that "such lines are not explicable by the theory of Cowley and Moodie".

The paper of ours[2] to which they refer contains not only a discussion of such effects as essential components of the concept of Fourier images but also a sequence of out-of-focus images obtained from an amplitude object with visible light which clearly demonstrates that such effects occur. The periodic object in our case was interrupted by a small internal non-periodic region, rather than by a sharp external boundary as in the case quoted by Hashimoto and Watanabe; but the progressive extension of the periodic grating image across the boundary as the order number of the Fourier image increases is clearly visible. Their electron micrographs may, in fact, be considered as further evidence in favour of our contentions at that time: they demonstrate that Fourier image phenomena are present and important in the electron microscope imaging of crystal lattices.

It appears that Hashimoto and Watanabe have considered not our theory of Fourier images but the simplification of it represented by their Fig. 2 and associated discussion, which ignores Fresnel diffraction effects and cannot, therefore, give an adequate account of the observation under discussion. This limitation should not, however, be attributed to our theory.

The Fourier image theory which we presented in our initial paper[2] was developed in detail only for periodic objects. It may be applied equally well to non-periodic objects. In either case, however, the theory is more conveniently developed on the basis of our reformulation of physical optics theory presented in later papers[3,4]. If we assume the incident radiation to be coherent and plane-parallel, the complex amplitude of the wave in an image out-of-focus by an axial distance, R, is given by :

$$\psi(x,y) = q(x,y) \bigstar \exp\{-ik(x^2 + y^2)/2R\} = \iint q(X,Y)\exp\{-ik[(x-X)^2 + (y-Y)^2]/2R\}\mathrm{d}X.\mathrm{d}Y$$

where $q(x,y)$ is the transmission function of the object. The intensity distribution is then given by $I(x,y) = \psi(x,y).\psi^*(x,y)$.

For the particular case of a crystal edge considered by Hashimoto and Watanabe, we may put :

$$q(x,y) = q_1(x,y).S(x) + S(-x)$$

where $q_1(x,y)$ is the periodic transmission function for an infinite, periodic crystal lattice and $S(x)$ is the step-function :

$$S(x) = \begin{cases} 0 \text{ for } -\infty < x < 0 \\ 1 \text{ for } 0 < x < \infty \end{cases}$$

If we put $q_1(x,y) = \frac{1}{2} + \frac{1}{2}\cos(2\pi x/a)$, which corresponds to an amplitude grating similar to that used by Hashimoto and Watanabe as an optical analogue, the calculated intensity distributions are as shown in Figs. 1*a*, *b* and *c* for the Fourier images of order $N = 0$, $N = \frac{1}{2}$ (that is, $R = a^2/\lambda$) and $N = 1$ (that is, $R = 2a^2/\lambda$). Figs. 1*a* and *b* clearly reproduce the relevant features of the intensity distributions, including the one relatively strong and two weak lines beyond the edge of the grating, visible in their Figs. 3*a* and *b* (ref. 1).

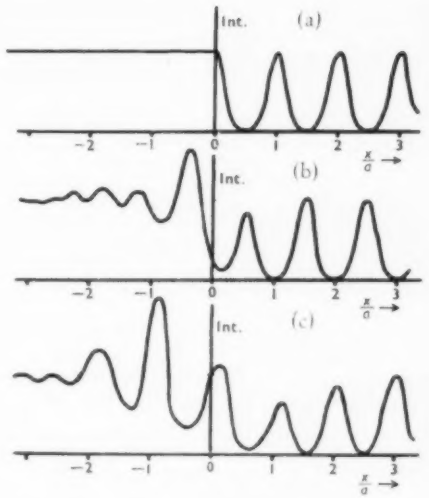

Fig. 1. The calculated intensity distribution at the edge of a periodic amplitude object of the form $\frac{1}{2} + \frac{1}{2}\cos(2\pi x/a)$, (*a*) in focus image (Fourier image of order $N = 0$); (*b*) out-of-focus (Fourier image of order $N = \frac{1}{2}$), and (*c*) Fourier image of order $N = 1$

In the same way we may calculate the intensity distribution to be expected at the boundary in an out-of-focus image of a copper phthalocyanine crystal if we put :

$$q_1(x,y) = \exp\{i\sigma\varphi(x,y)\}$$

where $\varphi(x,y)$ is the periodic function representing the projection of the potential distribution in the crystal lattice and σ is a constant. It has been established that, to a first approximation, thin crystals act as phase gratings for electrons[5] and a study has been made of the contrast in Fourier images of such

gratings[6]. We hope to publish elsewhere a more detailed account of the images of crystal lattices formed in electron microscopes.

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CHEMICAL ENGINEERING

A Rapid Method for the Determination of Tetramethyl Lead and Tetraethyl Lead in Petrol

The use of tetramethyl lead as anti-knock additive in petrol sets a new problem to the petroleum laboratories in connexion with the determination of these additives. The standard A.S.T.M. method *D* 526–56 cannot be used for the analysis of petrols containing a mixture of tetramethyl lead and tetraethyl lead or for the determination of lead in a sample containing alkylated lead additives.

We have tried to work out a rapid method for the qualitative determination of tetramethyl and tetraethyl lead in petrols. First, we tried to use a colour reaction with dithizone reagent. Dithizone in chloroform solution is added to the petrol. The mixture is shaken with water and a red colour appears in the organic phase. The reaction mechanism is apparently different for the tetramethyl and the tetraethyl lead. Tetraethyl lead seems to be less stable than tetramethyl lead; it hydrolyses more quickly and a red colour appears, whereas tetramethyl lead does not undergo any reaction. This test being extremely sensitive (limit 0·04γ), errors due to impurities in glass or water are likely to occur. It is also unsuitable for use with a red-coloured petrol.

We therefore tried another method, using petrol fractions obtained by distillation. Afterwards, we examined the different fractions by means of a Zeiss flame spectrophotometer *M4Q* at 406 mμ in order to determine the lead.

Generally, we have taken four fractions and the residue: initial boiling point to 100° C.; 100° to 125° C. (fraction containing the tetramethyl lead); 125° to 150° C.; 150° to 175° C.; and the residue (containing the tetraethyl lead). About 250 c.c. of petrol are distilled on a 'Vigreux' column (30 cm. in length), in 2 hr. We observed that the slower the distillation, the better the separation of the lead in the spectrophotometric determination.

To check the method, we used a platformate containing tetramethyl lead, a platformate containing tetraethyl lead and a platformate containing tetramethyl and tetraethyl lead. The figures in Table 1 indicate the galvanometer readings expressing the light intensity of the flame. The apparatus was standardized at a reading of 50 with a platformate containing 4·2 c.c. tetramethyl lead per Imperial gall. An oxy-acetylene flame is used. Only the figures in the horizontal lines of the table should be compared with each other. In this determination we did not consider the flame background of the different fractions. Since these results on lead distribution in known mixtures were reasonable, we examined commercial samples. The results are summarized in Table 2.

The petrols showing high readings in the 100° to 125° C. fraction were those giving aberrant results in the A.S.T.M. determination *D* 526–56. Moreover, these results tally with those advertised by petroleum companies. The method given here is simple and allows one to estimate tetramethyl and tetraethyl lead. Anti-knock quantitative analysis may be carried out in the usual way.

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Table 1

Fractions	Initial boiling point to 100° C.	100° to 125° C.	125° to 150° C.	150° to 175° C.	Residue
Platformate + tetramethyl lead	5	53·5	26	10	3
Platformate + tetraethyl lead	5	9·5	10	14	28
Platformate + tetramethyl lead + tetraethyl lead	18	33	19	21	37

Table 2

Fractions	Initial boiling point to 100° C.	100°–125° C. (tetramethyl lead)	125°–150° C.	150°–175° C.	Residue (tetraethyl lead)
Sample *A*, 'super'	4	47	30	20	7
Sample *B*, 'super'	7	41	37	25	14
Sample *C*, 'super'	9	44	36	19	17
Sample *D*, 'super'	8	38	25	—	8
Sample *E*, 'normal'	3	11	22	—	60
Sample *F*, 'super'	5	13	17	27	56
Sample *G*, 'normal'	4	6	8	14	69
Sample *H*, 'super'	3	12	24	24	50

CHEMISTRY

Influence of Chemical Isomerism on the Szilard–Chalmers Processes in Solids

The recent appearance[1] of a communication concerning the Szilard–Chalmers effect in *cis*- and *trans*- dichloro- *bis* (ethylenediamine) cobalt (III) nitrate prompts us to report the following results.

A considerable amount of work has been published in which processes associated to the Szilard–Chalmers effect are studied in solid-state complex combinations.

Less attention, however, has been given to the influence of chemical isomerism. The question arises whether in two chemical isomers the annealing of reactor irradiation damage occurs in the same way.

Zuber[2] was the first to study the Szilard-Chalmers effect in crystalline D-[Co en$_3$](NO$_3$)$_3$. After irradiation of the dextro complex and the addition of lævo isomer as carrier, he found by resolving [Co en$_3$](NO$_3$)$_3$ that, of 5 per cent annealed atoms after irradiation, only 4·5 per cent annealed as the dextro, and 0·5 per cent annealed as the lævo, isomer. It would be interesting to examine also the irradiated lævo isomer and to compare the behaviour of the two isomers. Recently, Saito and co-workers[3], investigating the behaviour of hot bromine atoms in cobalt complex salts, found no noteworthy differences in the yield of complexed radiobromine for *cis–trans* isomers. They did not examine the retention of radiocobalt.

Our attempts to find evidence of differences in the behaviour of chemical isomers in radiocobalt annealing processes were more successful. Cobalt complex combinations exhibiting geometrical, optical, hydration, ionization, or linkage isomerism were irradiated for 40 hr. in the *IF.A* reactor. The samples were irradiated in aluminium ampoules in air. The irradiation conditions were as follows: thermal neutron flux, $6{\cdot}0 \times 10^{11}$ *n*. cm.$^{-2}$ sec.$^{-1}$; fast neutron flux, $1{\cdot}75 \times 10^{11}$ *n*. cm.$^{-2}$ sec.$^{-1}$; gamma dose-rate, $1{\cdot}31 \times 10^{7}$ r. hr.$^{-1}$.

The fraction annealed after irradiation was determined via retention, using a well-known analytical technique for the separation of recoiled radiocobalt[4,5]. The results are given in Table 1, together with the difference in retention for a pair of isomers.

These investigations are continuing, but some conclusions may already be drawn. It appears that chemical isomerism plays an important part in the recombination process of recoil fragments occurring simultaneously with irradiation. This would be expected also when taking account of the influence of the steric factor on the annealing process. The difference in the spatial arrangement of groups corresponding to the same general formula certainly influences the interatomic distances and the internal field of the crystal. In addition, the influence of chemical groups which may act differently depending on their function in the molecule must be considered.

The greatest differences are observed with the hydration isomers, where the water of hydration has at first sight a reducing effect on the recoiled radiocobalt, a view which has been thought to apply to permanganate salts[6]. It is only known that water molecules behave differently when co-ordinated to cobalt. The geometrical isomers exhibit also considerably different retentions. It was observed that the *cis*-position is more advantageous, the annealing being lower for the *trans*-position where steric factors cause serious hindrance. For ionization and linkage isomers it was found that the chemical bond has some influence. The differences in the retention of lævo- and dextro-combinations though smaller are present. Here also the steric factor plays a part, although the differences do not act in the same direction.

Table 1. Retentions of Chemical Isomers after Reactor Irradiation

Isomerism	Chemical formula	Retention (*R* per cent)	Difference in retention (Δ*R* per cent)
Hydration	[Co(NH$_3$)$_4$(OH$_2$)Cl]Cl$_2$	68·2	39·0
	[Co(NH$_3$)$_4$Cl$_2$]Cl.H$_2$O	29·2	
Geometrical	*cis*-[Co en$_2$Cl$_2$]Cl	79·8	15·2
	trans-[Co en$_2$Cl$_2$]Cl	64·7	
	cis-[Co(NH$_3$)$_4$(NO$_2$)$_2$]NO$_3$	86·6	10·8
	trans-[Co(NH$_3$)$_4$(NO$_2$)$_2$]NO$_3$	75·8	
Linkage	[Co(NH$_3$)$_5$NO$_2$]Cl$_2$	71·1	6·8
	[Co(NH$_3$)$_5$ONO]Cl$_2$	77·9	
Ionization	[Co(NH$_3$)$_5$SO$_4$]Br	75·0	5·5
	[Co(NH$_3$)$_5$Br]SO$_4$	69·5	
Optical	D-[Co en$_3$](NO$_3$)$_3$	71·9	1·7
	L-[Co en$_3$](NO$_3$)$_3$	73·6	
	D-[Co en$_3$]Br$_3$.2H$_2$O	89·9	6·4
	L-[Co en$_3$]Br$_3$.2H$_2$O	83·5	

So far only qualitative investigations have been discussed. A systematic investigation involving analysis of recombination products and kinetic measurements is in progress and the results will be reported in due course.

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Interactions of NO_2–N_2O_4 and Niobium Dioxide (NbO_2)

The interaction of NO_2 and niobium dioxide (NbO_2) was studied as part of a general programme to investigate the oxidation chemistry of NO_2 with respect to its effect upon potentially non-stoichiometric oxides. Other oxides which have been investigated have shown that NO_2 may act as an oxidizing agent as well as a nitrating and nitriting agent. In addition, significant quantities of physically and chemisorbed NO_2 are always encountered in this type of interaction[1]. In a brief introductory study carried out on niobium oxide a number of significant points were uncovered which expand the present investigations.

Niobium dioxide was prepared by reduction in a stream of dry hydrogen at 950° C. The NO_2 was obtained from the Matheson Chemical Co. It was transferred to the vacuum line through a magnesium perchlorate trap, and was fractionated until the solid condensate was white. At all temperatures in the range of 100–500° C. and pressure of NO_2 of 0·014–65 cm. mercury the oxidation of the dioxide proceeded at a rapid rate, such that the composition of Nb_2O_5 was established nearly instantly. In many cases the dioxide acted as pyrophor, igniting and immediately producing the penta oxide. For the lower pressures and lower temperatures the oxidation proceeded more slowly and was noted to take several minutes for completion. In general, the rapidity of the reaction made a study of the kinetics impossible.

Analysis of the reacted product indicated that the composition of the final product was in all cases within 0·02 stoichiometric unit of the composition $NbO_{2.5}$. This was further confirmed by observing the optical reflectance in the ultra-violet. In addition

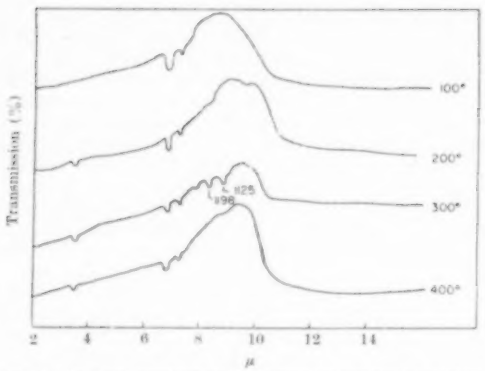

Fig. 1. Infra-red spectrum of the interaction product of niobium dioxide and nitrogen dioxide for various temperatures of interaction at a pressure of 65 cm. nitrogen dioxide

to the above stoichiometric ratio it was noted that a small amount of nitrogen was also incorporated in the oxide. At a pressure of 26·5 cm. mercury of NO_2 and in the temperature interval from 100 to 500° C. the stoichiometric ratio of nitrogen–niobium varied linearly with increasing temperature from 0·019 to 0·043 and at a $P_{NO_2} = 0·014$ cm. mercury the nitrogen content was within the limit of error of the method[2].

In an attempt to determine the origin of this incorporated nitrogen the infra-red spectra of the reacted material was obtained. This was done on a Perkin Elmer model 221 double-beam spectrophotometer. The spectra are partially reproduced in Fig. 1 for the interaction of NO_2 at 65·5 cm./mercury and Nb_2O_4 in the temperature-range of 100–500° C. Absorption peaks may be seen at ~ 3·5, 6·8, and 7·3μ due to interference from the 'Nujol' mulling agent. Secondly, a broad band is in evidence which begins at about 10·5μ. This is most probably due to the Nb–O stretching frequency[3,4]. Finally, bands may be seen at ~ 7·8, 8·3, 8·8 and 9·6μ. It is felt that the bands at 7·8 and 9·6 are probably due to the presence of some form of ionic nitrate[5] as these bands have been found to be characteristic of ionic nitrates in general. The bands at 8·3 and 8·8 appear to be due to the NO_2 group, in the form of strongly chemisorbed nitrogen dioxide or as the nitrite group[6]. It should be noted that in both these cases the presence of these species occurs at an extremely low concentration and thus does not demonstrate the inherent basic character in niobium dioxide.

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Dissociation Energy of Aluminium Monobromide

In a recent review[1] of the dissociation energies of the gaseous monohalides of boron, aluminium, gallium and thallium, it was concluded that the best value for D_0'' (aluminium monobromide) is 105 k.cal. mole^{-1}. Dr. P. Gross has now kindly directed my attention to the work of Semenkovich[2], who has determined the standard heat of formation of gaseous aluminium monobromide by a thermochemical method similar to that used by Gross, Campbell, Kent and Levi[3] for aluminium monofluoride and monochloride. Semenkovich obtains $Q_f(AlBr_g) = +1·1$ k.cal. mole^{-1}. With $\Delta_f H(Al) = 77·4$, $Q_f(Br_g) = 26·71$, and $D_{298}'' - D_0'' = 0·85$, $D_0''(AlBr) = 102·2$ k.cal mole^{-1}. As with AlF and AlCl, this value is a little lower than two of the spectroscopic estimates from the state $A^1\Pi$, which, for AlBr, are 106·9 k.cal. by extrapolation, and >104·4 k.cal. from the highest observed vibrational level: it is, however, consistent with a predissociation limit which leads to $D_0'' \leqslant 105·7$ k.cal.

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Triplet Bands of Carbon Monoxide: the System $e\,^3\Sigma^- - a\,^3\Pi$

Some years ago, in a study of the triplet system, $d(^3\Pi) - a^3\Pi_r$ of carbon monoxide, Herman and Herman[1] observed a progression of bands of similar appearance which they assigned to a new system. They suggested that the upper state of this system was d and that the lower state was a new triplet-level, lying close to $a^3\Pi$. Later work[2,3] on the forbidden systems of carbon monoxide observed in the absorption spectrum in the Schumann region has provided detailed information about some of the triplet-levels, and the object of this communication is to show that the Herman system arises in fact from the transition $e\,^3\Sigma^- - a\,^3\Pi_r$.

In Table 1, the second column gives values of band-origins of the $e - X$ system[2]. Positions of the band-heads of the Herman system[1] are given in columns three and four. The results of subtracting column four from two are given in column five. These figures are as constant as could be expected, and indicate that the bands form a progression involving the levels $v' = 2$ to 7 of $e\,^3\Sigma^-$. The mean value for the height of the lower level above $v = 0$ in the ground-state $X\,^1\Sigma^+$ is 48,520·$_3$ cm.$^{-1}$.

Table 1

v'	e–X ν_0	e–a λ	e–a ν	a–X ν
7	71,926·5	4,270·8	23,408·3	48,518·2
6	70,966·2*	4,454·5	22,442·9	523·3
5	69,986·4	4,657·2*	21,465·9*	—
4	68,987·9*	4,885·0	20,465·1	522·8
3	67,970·3	5,140·3	19,448·7	521·6
2	66,933·3	5,428·3	18,416·9	516·4

* Interpolated value.

The measurements of band-heads given in Table 1 refer to the longest wave-length heads of groups of three. For the $v' = 2$ and $v' = 3$ bands, further measurements are available[4]:

5428·3 Å.	18,416·9	cm.$^{-1}$ 46·9	5140·3 Å.	19,448·7	cm.$^{-1}$ 46·3
14·5	463·8	41·0	28·1	495·0	45·3
02·5	504·8		16·2	540·3	

The mean separation between adjacent heads is thus about 45 cm.$^{-1}$ and the origin of the lower state may be estimated to lie at $48{,}520\cdot_5 - 45 = 48{,}475\cdot_5$ cm.$^{-1}$ above $X\ ^1\Sigma^+$. This estimate is in excellent agreement with the value of ν_{00} for $a^3\Pi - X^1\Sigma^+$ obtained from the rotational analysis[5] of the Cameron bands, namely, $48{,}473\cdot9_7$ cm.$^{-1}$.

It seems, therefore, quite certain that the Herman bands form the $v' - 0$ progression in the transition $e\ ^3\Sigma^- - a\ ^3\Pi$. No doubt other bands of this system remain to be found at longer wave-lengths.

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Identification of the Radical $\cdot CH_2(CO_2H)$

In recent years a number of free radicals trapped in irradiated solids have been identified from their electron-spin resonance spectra. In particular, radicals of the form $X\dot{C}HCO_2H$ or $X\dot{C}HCO_2^-$ are known with $X = CH_3$ (ref. 1), NH_3^+ (ref. 2), OH (ref. 3), CO_2H (ref. 4), Cl (Pooley, D., and Whiffen, D. H., unpublished work), CH_3CO_2H (ref. 5), and $CH_3.CH_2CO_2H$ (unpublished work by A. H., J. R. M. and D. H. W.). Hitherto, however, the parent radical $\cdot CH_2(CO_2H)$ has remained unidentified. This radical has now been identified in γ-irradiated malonic acid, $CH_2(CO_2H)_2$. McConnell *et al.*[4] have fully investigated the radical $\dot{C}H(CO_2H)_2$ which is also formed when malonic acid is γ-irradiated; they reported that lines not due to $\cdot CH(CO_2H)_2$ appeared in the spectra of freshly irradiated crystals, and could be removed by heating the crystals to 50° C. for 24 hr.

A detailed study of the spectrum of irradiated malonic acid was undertaken using an electron resonance spectrometer operating at 9,000 Mc./s. A single crystal of malonic acid was γ-irradiated at liquid-nitrogen temperature. Its room-temperature spectrum indicated that at least three radicals were present. For a general orientation of the crystal with respect to the magnetic field, all three radicals have different g values, and each has a spectrum symmetrical about its own centre. If the hyperfine structure of the spectrum of each radical can be analysed, it is possible to identify the radical. For some crystal orientations, however, exact analysis is difficult because of overlapping of the spectra of different radicals. The spectrum of a freshly irradiated single crystal of malonic acid consisted of two exceedingly strong and narrow lines due[4] to the radical $\cdot CH(CO_2H)_2$. In addition, we observed four sharp lines of equal intensity approximately one-fifth as strong as the spectrum of $\cdot CH(CO_2H)_2$. A third radical was also present, but its spectrum was still weaker and the radical has not yet been positively identified.

The spectrum of intermediate intensity indicates the presence of a radical in which there is hyperfine interaction with two hydrogen nuclei. This spectrum could be analysed for a sufficient number of orientations to obtain a complete coupling tensor for each hydrogen atom. However, the precision is less than that which would be attainable if this were the only radical present. The principal values of the coupling tensor of one hydrogen atom were −91, −56 and −30 Mc./s., and for the other −92, −59 and −37 Mc./s. These values are essentially those to be expected for a hydrogen atom attached directly to the free radical centre[2,4,6]. They have therefore been given a negative sign, although this is not obtained directly from the spectra. The coupling tensors identify the radical as $\cdot CH_2(CO_2H)$, since no other radical with two hydrogens on the free-radical carbon atom is anticipated from the irradiation of malonic acid. The slight differences between the two tensors are less than the probable experimental error (±4 Mc./s.), although the two hydrogen atoms are not in crystallographically equivalent positions in the trapping site, and their coupling tensors need not, therefore, be absolutely identical. It appears that the methylene group ($-\dot{C}H_2$) in the radical is not rotating about the C—C bond, since free rotation would lead to a spectrum having three hyperfine lines with intensity ratios 1 : 2 : 1 for all crystal orientations.

It is expected[2,6] that the least negative, intermediate, and most negative principal values of the coupling tensor will occur for directions parallel to the C—H bond, perpendicular to the plane of the radical, and in the plane of the radical but perpendicular to the C—H bond, respectively. The intermediate axes for both tensors therefore should be parallel to each other. This was found to be the case, the experimental value for the angle between the intermediate axes of the two tensors being 4° with an error of approximately 5°. The major and minor axes of each tensor should intersect at an angle equal to the HCH angle. This angle was calculated from the tensors to be 116 ± 5°. In a planar radical, this angle would be 120° for strict sp^2 hybridization, although van der Waals repulsion between the hydrogen atoms and the carboxylic acid group might give rise to a slight reduction in this value.

The electron-resonance spectra of irradiated malonic acid thus support a planar structure for the substituted methyl radical, in agreement with previous work[7] on the methyl radical itself.

This investigation was undertaken as part of the programme of the Basic Physics Division of the National Physical Laboratory, and will be published in detail elsewhere. This report is published by permission of the Director.

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BIOCHEMISTRY

Fatty Acid Specificity for the Esterification of Vitamin A and Cholesterol by Intestinal and Pancreatic Enzymes in Rats

Vitamin A and cholesterol esters have been shown to undergo extensive hydrolysis in the lumen of the small intestine during the process of absorption; they are re-esterified to appear in the lymph mostly as esters[1,2]. However, the vitamin A esters of the lymph, blood and liver of the rat are formed by long-chain fatty acids[3] and in the normal rat liver, probably as palmitates[4]. On the other hand, cholesterol esters are usually made up of poly-unsaturated fatty acids in the lymph and blood of rats[5]. For the absorption of the two lipid materials, the enzymes of the pancreas have been largely implicated, while not much attention has been paid to the possible role of the mucosal enzymes. From the behaviour of the mucosal enzymes, as presented here, it appears that probably these enzymes play a more important part in the re-esterification of the two lipid materials during their absorption.

Acetone-dried powder was prepared from the intestinal mucosae and pancreas of normal stock rats of this Institute by grinding the tissues in 10 vol. of acetone pre-cooled to −15°. The powder was suspended in cold distilled water in the proportion of 1 gm. powder per 10 ml. water for 1 hr. and was then centrifuged for 10 min. at 10,000*g* in the cold. The clear supernatant liquid was suitably diluted and used as the source of the enzymes. The reaction mixtures for cholesterol esterification contained 5 μmoles of free cholesterol and 10 μmoles of the given fatty acid in 0·5 ml. of ethanol, 3 ml. of Michaelis veronal buffer (0·1 *M*), *p*H 6·1, 25 mgm. of sodium taurocholate and the enzyme extracts representing 10 mgm. of pancreatic or 25 mgm. of intestinal powder. The final volume was made up to 5 ml. and incubation was for 30 min. for pancreas and 60 min. for intestine at 37°. The reaction mixtures for vitamin A esterification contained 1 μmole of vitamin A alcohol and 2 μmoles of the given fatty acids in 0·5 ml. ethanol, 3 ml. of Michaelis veronal buffer (0·1 *M*), *p*H 6·6 and the enzyme extract representing 2 mgm. of pancreatic or 5 mgm. of intestinal powder. The final volume was made up to 5 ml. and both were incubated for 30 min. at 37°. The reaction mixtures were extracted twice with light petroleum ether (40–60°) after stopping the reactions by the addition of 5 ml. of ethanol. We have been using chromatographic procedures for the separation of vitamin A ester and alcohol, and we have found that the same method can be used for the quantitative separation of free and esterified cholesterol also. The two forms of vitamin A and cholesterol were, therefore, separated on alumina columns[6] and estimated as described previously[7].

Results summarized in Table 1 clearly show that both pancreatic and intestinal enzymes esterify cholesterol preferentially with unsaturated fatty acids. Our findings with the pancreatic enzymes agree broadly with the earlier reports of Hernandez and Chaikoff[8] and Swell *et al.*[9], who have shown that the presence of unsaturation in the fatty acid is necessary for the effective esterification of cholesterol by the pancreatic enzymes. However, according to Hernandez and Chaikoff[8], while oleic and linoleic acids showed almost the same rates of esterification, linolenic acid was only 13 per cent as active as oleic acid, and our results with the pancreatic enzymes show linoleic and linolenic acids to be 68 and 40 per cent as efficient as oleic acid. In contrast, as demonstrated here, the mucosal enzymes exhibit progressively increased esterification with increase in the unsaturation of the fatty acid. If the pancreatic enzymes were to re-esterify cholesterol for its transport during absorption, the oleate should be the major ester in the lymph and blood, but in these tissues the cholesterol is found esterified mostly with polyunsaturated fatty acids[10–12]. It thus seems clear that the mucosal enzymes, rather than the pancreatic enzymes, are responsible for the re-esterification of cholesterol during absorption.

Table 1. Fatty Acid Specificity for the Esterification of Vitamin A and Cholesterol by the Enzymes of Intestine and Pancreas of Rats

Fatty acid	μmoles cholesterol esterified/mgm. protein/hr.		μmoles vitamin A alcohol esterified/mgm. protein/hr.	
	Pancreas	Intestine	Pancreas	Intestine
Acetic	0·0	0·0	3·0	2·3
Butyric	0·0	0·0	2·3	1·5
*Iso*valeric	0·0	0·0	2·3	2·3
Caproic	0·0	0·0	2·3	1·5
Lauric	60·0	7·5	938·0	285·0
Myristic	40·0	5·0	868·0	142·5
Palmitic	47·5	5·5	898·0	159·0
Stearic	50·0	5·7	798·0	139·5
Oleic	1,313·0	50·0	840·0	130·5
Linoleic	885·0	71·5	854·0	135·8
Linolenic	515·0	82·0	882·0	132·0

Regarding the esterification of vitamin A, neither tissue showed any preference for unsaturation, and it was effectively esterified with fatty acids containing more than 12 carbon atoms by both the tissues. It should be mentioned here that Pollard and Bieri[13] had similar experience with chick pancreas. This again would explain the presence of higher fatty acid esters of vitamin A in the blood and lymph of rats[3].

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In vitro Decarboxylation of Tryptophans by Mammalian Decarboxylase

Twenty-two tryptophans have been examined in order to check the specificity of the so-called 5-hydroxytryptophan decarboxylase[1,2], and at the same time to see whether any of these compounds could be decarboxylated at a rate similar to that known for 5-hydroxytryptophan (5-HTP). The present work was intended as preliminary to further investigations on the possibility of non-biogenic tryptophans interfering in the biosynthesis, actions and metabolism of endogenous 5-hydroxytryptamine (5-HT), especially of brain 5-HT.

The tryptophans examined were the following: L-tryptophan, DL-5-hydroxytryptophan, DL-4-hydroxytryptophan (4-HTP), DL-6-hydroxytryptophan, DL-7-hydroxytryptophan, DL-2-hydroxytryptophan, DL-α-*iso*-5-hydroxytryptophan, DL-5-methyltryptophan, DL-5-methoxytryptophan, DL-5-benzyloxytryptophan, DL-5-nitrotryptophan, DL-5-aminotryptophan, DL-5-hydroxy-β-methyltryptophan, DL-5-hydroxy-N,N-dimethyltryptophan, DL-5-hydroxy-6-methoxytryptophan, DL-5-hydroxy-2-methyltryptophan, DL-5-benzyloxy-6-methoxytryptophan, DL-5-hydroxy-N-acetyltryptophan, DL-5-acetoxy-N-acetyltryptophan, DL-4-methyltryptophan, DL-4-benzyloxytryptophan, DL-6-benzyloxytryptophan.

The enzyme preparations were obtained by centrifugation of homogenates of different guinea pig, rat, mouse and rabbit tissues in a Spinco preparative centrifuge, at 15,000 r.p.m. Decarboxylation was carried out in a conventional Warburg apparatus, at 38° C. and *p*H 7·4. The flasks contained 4 m.moles of the substrate amino-acid, 50 μmgm. pyridoxal phosphate, 0·07 μmole phosphate buffer, *p*H 7·4, and 2 ml. of the enzyme preparation, corresponding to 1 gm. fresh tissue. The total volume in the flasks was 2·4 ml. Carbon dioxide produced was determined 15 min. after the addition of 0·2 ml. of *N* sulphuric acid.

Of the tryptophans examined only 5-HTP, 4-HTP, 5-hydroxy-N-acetyltryptophan and 5-acetoxy-N-acetyltryptophan were found to be decarboxylated using the above conventional, and not very sensitive, Warburg technique.

However, as clearly shown by *in vivo* studies, decarboxylation of 5-hydroxy-N-acetyltryptophan and 5-acetoxy-N-acetyltryptophan was preceded by their hydrolysis to 5-HTP. Thus, only 5-HTP and 4-HTP actually acted as substrates for the decarboxylase.

Table 1 shows the results of a 30-min. incubation of DL-5-HTP, DL-4-HTP and dopa (3,4-dihydroxyphenylalanine was used only for the sake of comparison) with enzyme preparations from various tissues.

The carbon dioxide expected for complete decarboxylation was 44·7 μl. Addition of a mixture of 4-HTP and 5-HTP to a guinea pig kidney decarboxylase preparation led to a stoichiometric liberation of carbon dioxide consistent with the decarboxylation of both substrates.

The enzymic activity of the guinea pig kidney preparation was strongly inhibited, at *p*H 6·8, by the addition of α-methyldopa (8 μmoles), caffeic acid (8 μmoles) and cynarine (8 μmoles). However, inhibition of decarboxylation of 5-HTP was more complete than that of 4-HTP and dopa.

In sharp contrast to dopa, neither 5-HTP nor 4-HTP was attacked by bacterial decarboxylase (acetone-dried cells of *Streptococcus faecalis* R.).

Table 1. *In vitro* Decarboxylation of 5-HTP, 4-HTP and Dopa by Enzyme Preparations from Different Tissues

Enzyme preparation	Substrate	Carbon dioxide formed in 30 min. (μl.)
Guinea pig liver	5-HTP	32·0
" " "	4-HTP	39·0
" " kidney	5-HTP	42·2
" " "	4-HTP	33·0
" " "	Dopa	41·5
" " intestine	5-HTP	37·5
" " "	4-HTP	36·5
" " "	Dopa	40·0
Rat intestine	5-HTP	0
" "	4-HTP	0
" "	Dopa	0
Mouse brain	5-HTP	12·5
"	4-HTP	20·0
Rabbit lung	5-HTP	0
" "	4-HTP	0

The above experimental results show that the so-called 5-HTP-decarboxylase is not an enzyme specific to 5-HTP, and that 4-HTP may be the precursor amino-acid of the 4-hydroxyindolealkylamines (psilocin and psilocybin) occurring in the living organism. In a recent paper, Udenfriend, Lovenberg and Weissbach[3] also suggest that the existence of seperate dopa and 5-HTP decarboxylase should be withdrawn.

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An Evaluation of the Use of Digitonin for the Analysis of Fæcal Sterols

Numerous reports have appeared in the literature dealing with the analysis of fæcal sterols[1–3]. Before the complexity of the sterol mixture of faeces was appreciated[4], a commonly employed procedure for the analysis of coprostanol was based on the difference between the total sterol determined by gravimetric analysis of the digitonide of the mixture and the amount of cholesterol or 'chromogenic sterol' calculated from the colour produced with the Liebermann Burchard reagent[1,2]. While many investigators recognize that the chromogenic property of coprostanol will introduce an error in the analysis if coprostanol is determined as cholesterol using the

digitonide precipitation procedure, a more serious error arises from the fact that the digitonide of coprostanol is significantly soluble in many of the solvent mixtures used (for example, the Sperry–Webb determination for cholesterol[5]). This unusual solubility property of coprostanol digitonide was recognized early by Dam[6] when he reported that in contrast to cholestanol digitonide, the digitonide of coprostanol was significantly soluble in methanol, a property which allowed the crude separation of the two sterols. This information prompted us to study the solubility of coprostanol digitonide in the solvent mixture routinely employed in the Sperry–Webb procedure and to compare our results with cholesterol digitonide as a reference.

Cholesterol used for the present work was obtained from Armour and Co. and purified via the dibromide (m.p. 147–8°). The coprostanol was obtained from rat faeces and was previously isolated in this laboratory[7] as a chromatographically pure zone on silicic acid/'Celite'. To eliminate the possibility of the presence of coprostan-3α-ol, the coprostan-3β-ol was further purified through the digitonide (Nutritional Biochemical Company), washed with acetone/ether (1 : 2) and ether, and regenerated as the 3β-sterol by cleavage of the digitonide with pyridine (m.p. 98–99° C.). Standard solutions of cholesterol and coprostanol were prepared in absolute ethanol/acetone (1 : 1) and suitable aliquots (300 μgm.–1,400 μgm.) were analysed in triplicate as follows: The aliquots were transferred to either a centrifuge tube or a colorimeter tube and the ethanol–acetone removed under vacuum at 50–60° C. To the samples in the centrifuge tubes, 2 or 4 ml. of absolute ethanol/acetone (1 : 1 v/v) were added. A drop of 10 per cent acetic acid was added to each tube, and either 1 ml. or 2 ml. of a 0·5 per cent solution of digitonin in 50 per cent ethanol brought the final volume to 3 or 6 ml. respectively. The mixture was heated for 15 min. in a water-bath at 50° C. and allowed to stand for 18–24 hr. In every case, the 5 or 10 mgm. of digitonin added was in excess of the theoretical requirement. The digitonides were washed and dried exactly as described by Sperry–Webb[5]. After the removal of ethanol–acetone and ether from the pooled washings, the remaining sterol was partitioned between ether and water. The ether extract was washed several times with water. The mixture was taken to dryness *in vacuo*, and the recovered sterol determined quantitatively as described here. The quantity of cholesterol and coprostanol was determined colorimetrically in 2 ml. of glacial acetic acid and 4 ml. of Liebermann–Burchard reagent using suitable constants as previously described[1]. As a control the original corresponding aliquot was analysed colorimetrically by the direct addition of 2 ml. of glacial acetic acid and 4 ml. of Liebermann–Burchard reagent.

In the second series, mixtures of coprostanol and cholesterol were analysed in various proportions. In every case the mixtures totalled 800 μgm. of sterol. The sterols were analysed by the same method as described above and compared in each case with the absorbancy obtained for the appropriate control.

The results (Table 1) confirmed the complete recovery of cholesterol digitonide in all concentrations employed for either final volume. The photometric reading of coprostanol digitonide at the 300-μmgm. level is inaccurate and is omitted. The

Table 1. Recovery of Cholesterol and Coprostanol Digitonides in the Sperry–Webb Solvent Mixture

Weight of sterol	Recovery of digitonide (percentage of total sterol)			
	Cholesterol		Coprostanol	
μgm.	3 ml.*	6 ml.*	3 ml.*	6 ml.*
300	100	100	—	—
600	100	100	97·1	65·0
800	100	100	78·6	67·9
1,000	100	100	80·8	63·0
1,400	100	100	70·6	59·6

* The volumes indicated refer to the final volume of the solvent mixture.

Table 2. Recovery of Mixed Cholesterol and Coprostanol Digitonides in the Sperry–Webb Solvent Mixture

Composition of sterol mixture* (per cent)		Recovery of mixed digitonides (percentage of total sterol)
Coprostanol	Cholesterol	
0	100	100
25	75	89·4
50	50	88·6
75	25	78·9
100	0	78·6

* Total sterol, 800 μgm., 3 ml. of Sperry–Webb solvents.

recovery of coprostanol of moderate to high levels in 3 ml. of solvent was found to vary from 97·1 to 70·6 per cent. When the final volume was doubled, an appreciable decrease in recovery was observed for comparable concentrations of coprostanol (65·0–59·6 per cent).

Analysis of the mixtures of coprostanol and cholesterol revealed that increasing the proportion of coprostanol resulted in a decrease in the recovery of the mixed digitonide (89·4–78·6 per cent).

The quantity of sterol recovered from the Sperry–Webb washings was found to correspond in each case to that amount of sterol not precipitated by digitonin. Our present results suggests that incomplete precipitation of coprostanol digitonide in the solvents of the Sperry–Webb procedure or equivalent solvents may account for some of the observed quantities of 'non-3β-hydroxy faecal sterols'[8]. Thus, it is our opinion that faecal sterol analysis with the above limitations can be more successfully carried out by a suitable chromatographic procedure as previously described[4]. Recent developments in the separation of sterols by quantitative gas chromatography[9] have stimulated much interest in the applicability of this technique to quantitative sterol determinations.

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Action of Trypsin on Bence-Jones Protein Derivatives

It is well known that the proteolytic enzyme trypsin fails to hydrolyse native proteins, or hydrolyses them to only a very small extent. The denaturation of protein substrate is therefore a customary preliminary operation in all work involving the action of trypsin on proteins. We report here the effect of trypsin on some chemical derivatives of a pure de-ionized[1] Bence-Jones protein isolated in large amounts from the urine of a single patient.

The protein was oxidized with performic acid, as described by Harrington and Schellman[2], treated with sulphite by the Swan technique as modified by Bailey and Cole[3], reduced with mercaptoethanol in 8 *M* urea as suggested by White[4], or with sodium borohydride[5]. The completeness of reduction was checked by employing the *p*-chloromercuribenzoate spectrophotometric titration described by Sela *et al.*[6]. The reduction products were directly digested or previously carboxymethylated with iodoacetic acid or treated with iodoacetamide.

The trypsin employed was a salt-free twice crystallized commercial preparation (Sigma Lot *T* 30*B*-056).

All digestion experiments were performed in a *p*H-stat (model *TTT–1A* Radiometer, Copenhagen) employing 100 mgm. of the protein or its derivative in 4 ml. of de-ionized water brought to *p*H 8·00 with 0·2 *N* sodium hydroxide; 5 mgm. of trypsin in 0·5 ml. of 0·001 *N* hydrochloric acid added in five 0·1-ml. aliquots, each every 15 min. The *p*H was maintained at 8·00 with 0·2 *N* sodium hydroxide; the temperature was 30° C.

The molecular weight of this Bence-Jones protein was assumed to be 36,000 on the basis of physicochemical measurements and of quantitative N-terminal amino-acid determinations.

The results obtained are presented in Fig. 1. It is easy to see that the opening, either oxidative or reductive, of the disulphide bonds leads to the same sensitivity toward trypsin. Even the digestion-rates for the derivatives are similar, though the rate for the simply reduced protein (curve 4) is slower, owing probably to the combination of the free sulphydryl groups to form aggregates.

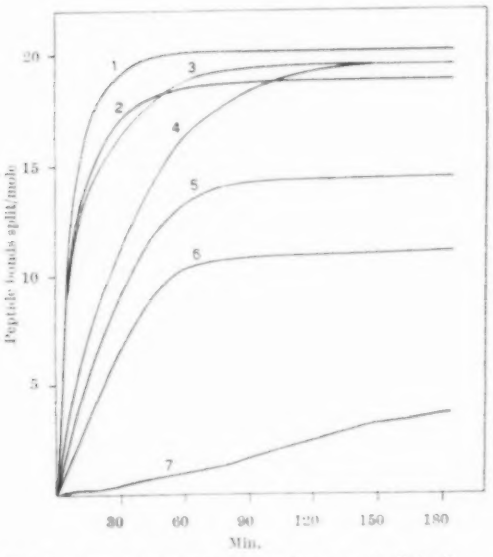

Fig. 1. Tryptic hydrolysis of Bence-Jones protein derivatives. Curve 1, sulphite-treated; curve 2, performic acid oxidized; curve 3, reduced and carboxymethylated; curve 4, reduced; curve 5, in urea 2 *M*; curve 6, in urea 1 *M*; curve 7, native

Bence-Jones protein in urea shows an increasing sensitivity to trypsin with increase of urea molarity (see curves 5 and 6).

It is concluded from the above results that anything which leads to a cleavage of disulphide bonds probably leads to a very similar configuration of the molecule, and that the urea-induced modifications, which respect the integrity of disulphide bridges, result in a lesser sensitivity to trypsin.

The use of tryptic digestion as an auxiliary tool for configurational studies on protein molecule is suggested.

Details of the above work and other results will be published fully elsewhere.

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Apparent Reversal of Xanthine Oxidase Action in *Chlorella vulgaris* starved of Nitrogen

In previous publications[1–3] a marked stimulation of the endogenous respiration of *Chlorella vulgaris* and other organisms by numerous purines and purine analogues was described. Several lines of evidence led to the suggestion that these results were best explained by a cyclical oxidation and reduction of the purines, coupled to oxygen on one hand and to the oxidation of fatty acids on the other. This assigns to xanthine oxidase a role in terminal oxidation. This communication presents evidence for an apparent reduction of oxidized purines in *Chlorella*, lending support to the existence of a purine oxidation-reduction cycle.

Chlorella vulgaris (ATCC 11468) was grown and harvested as previously described[1]. Washed cells were suspended in 0·067 *M* phosphate buffer, *p*H 6·0, and incubated with 10^{-4} *M* reduced purines (hypoxanthine or 8-azahypoxanthine) for 15 min. before the oxidized purines labelled with carbon-14 were added (final concentration 10^{-4} *M*). After shaking the suspensions in the dark for another 30 min. solid trichloracetic acid was added to a final concentration of 5 per cent. The cell suspensions were centrifuged after 30 min. standing, and this extraction step was repeated twice. Authentic purines or azapurines were added as carriers. The extracts, freed of trichloracetic acid, were concentrated *in vacuo*.

Chlorella cells which had been exposed to hypoxanthine and then to uric acid-2-^{14}C were extracted. Fig. 1 shows the elution pattern of this extract from

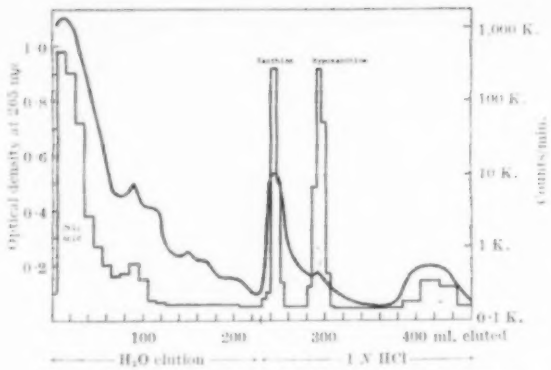

Fig. 1. Distribution of carbon-14 activity in the eluates from a 'Dowex-50(H⁺)' column. An extract of cells which had been incubated with uric acid-2-^{14}C, together with uric acid, xanthine and hypoxanthine was applied. Boxed line, optical density; continuous line, radioactivity

a 'Dowex 50' column[4]. In addition to uric acid, considerable radioactivity was found in xanthine. Two other compounds also showed activity and were probably oxidation products of uric acid. Uric acid is oxidized rapidly in this system[4], and allantoin is eluted from this column directly following uric acid.

The peak corresponding to xanthine was freed of hydrochloric acid by evaporation to dryness *in vacuo*. The radioactivity in this peak co-chromatographed with authentic xanthine in the following solvent systems which were run in a descending manner: *n*-butanol/pyridine/water (70 : 30 : 10) run for 72 hr., *n*-butanol saturated with water (64 hr.), and *n*-butanol/methyl-ethyl-ketone/triethylamine/water (20 : 20 : 2 : 10) for 64 hr. The radioactivity could not be separated from the xanthine spot by high-voltage paper electrophoresis in 0·075 *M* phosphate buffer, *p*H 7·5.

Following exposure of *Chlorella* to 8-azaguanine-2-^{14}C, a very small amount of radioactivity was detected by paper chromatography of the cell extract in the 8-azahypoxanthine spot. These chromatograms were developed in an ascending manner in 2 *N* hydrochloric acid/*iso*propanol (35 : 65)[5]. However, the chromatograms were overloaded with azaguanine and azaxanthine and a second separation in the same solvent was necessary to obtain radiochemically pure azahypoxanthine. The doubly chromatographed azahypoxanthine was eluted and further rechromatographed in butanol saturated with water and also in butanol, pyridine, water. The material was also subjected to electrophoresis in 0·05 *M* sodium bicarbonate–sodium carbonate buffer, *p*H 9·85. With both methods the radioactivity was not resolved from the ultra-violet light-absorbing spot of 8-azahypoxanthine.

In addition to the previously demonstrated oxidation of the purines in *Chlorella*[6], these results show that a mechanism also exists whereby purines are reduced. These reduced products were present in small amounts and, therefore, the steady state for these reactions must be far towards oxidation. The level of radioactivity in hypoxanthine was probably too low for unequivocal detection.

The only previous report of a reversal of xanthine oxidase is that of Whitely and Ordal[7]. However, in this case the reaction was carried out in an atmosphere of hydrogen. My results are not sufficient to exclude the possibility that the apparent reversal of xanthine oxidase took place via a nucleotide cycle such as that described recently by Magasanik and Karibian[8]. Nevertheless, it is difficult to envisage the involvement of histidine biosynthesis in the purine effect, since this effect is dependent on nitrogen starvation of the cells and takes place in the absence of any added nitrogen sources. Furthermore, the instantaneous response of respiration to added purines[1] would not suggest that there is an initial conversion of the purines to the nucleoside or nucleotide stage. It has been found in results, which will be presented elsewhere, that the substrates for the purine-stimulated respiration are the storage lipids of the cells. It is tempting to speculate that the reduction of the purines is coupled in some way to a step in the oxidation of the lipids. The resulting cycle could serve as a mechanism for a terminal electron-carrying system.

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Action of Glutamic Acid and Glutathione Analogues on the *Hydra* Glutathione-Receptor

REDUCED glutathione (GSH) is known to activate surface receptors of *Hydra*, resulting in the co-ordinated feeding reflex[1]. Loomis's demonstration that asparthione (β-aspartyleysteinylglycine) did not activate the feeding reflex suggests that the γ-glutamyl moiety is essential for the action of GSH[1]. Furthermore, the demonstration by Cliffe and Waley that ophthalmic acid (γ-glutamyl-α-amino-*n*-butyrylglycine) activated the feeding reflex shows that the sulphydryl group is not necessary for the action of GSH on *Hydra*[2]. The present work was undertaken to characterize further the structural features of the tripeptide which are necessary for the activation of the GSH-receptor. In this series of experiments we demonstrate that either glutamic acid or glutamine act as competitive inhibitors of GSH. In addition, analogues of the GSH tripeptide were found either to activate or inhibit competitively the feeding reflex, depending on the size of the group substituted for the thiol.

The activity of the feeding reflex is expressed as previously described[2], and the experiments were carried out with the following modifications: (1) only *Hydra* starved for two days were used; (2) all experiments were carried out in a solution consisting

Table 1. Activation or Inhibition of the GSH-Receptor

Compound	Duration of the feeding reflex (min.)		
	Compound alone	Compound + 10^{-6} *M* GSH	Compound + 10^{-5} *M* GSH
Control, no analogue added		28·3	35·2
Glutamic acid 10^{-3} *M*	0	0·8	22·6
Glutamine 10^{-3} *M*	0	0	23·1
Ophthalmic acid 10^{-3} *M*	31·6		
S-methylglutathione 10^{-3} *M*	29·2		
Asparthione 10^{-3} *M*	0	0	32·7
S-Acetylglutathione 10^{-3} *M*	0·3*	3·3	31·1
γ-L-Glutamyl-L-sulphi-alanylglycine 10^{-3} *M*	0	0	15·7
Oxidized glutathione 10^{-3} *M*	0	2·3	23·1

* A small amount may be hydrolysed at these conditions.

of 10^{-2} *M* calcium chloride, 10^{-1} *M* sodium chloride and 10^{-2} *M* histidine buffer, *p*H 6·2.

The results (Table 1) demonstrate that 10^{-5} *M* glutamic acid inhibited the feeding reflex which was activated by 10^{-6} *M* GSH. Increasing the GSH concentration to 10^{-5} *M* reversed this inhibition; thus, the inhibition is thought to be competitive. Glutamine, at 10^{-3} *M*, also was shown to inhibit competitively. Not inhibitory were cysteine, glycine, α-ketoglutaric acid, glutaric acid, pyroglutamic acid, aspartic acid, asparagine, and glycylglycine.

Also shown in Table 1 are the actions on *Hydra* of different GSH analogues. Only two, ophthalmic acid and S-methylglutathione, activated the feeding reflex in the absence of GSH. Analogues having large substituents at the thiol position, as in the case of S-acetylglutathione, oxidized glutathione, or γ-L-glutamyl-L-sulphi-alanylglycine, did not activate the feeding reflex. In contrast, 10^{-4} *M* concentrations of the analogues were potent inhibitors of GSH at 10^{-6} *M*. These inhibitions were partially or completely overcome by increasing the GSH concentration to 10^{-5} *M*.

It is of interest to compare the activity of GSH analogues on two different systems requiring GSH: the enzyme glyoxalase, and the GSH-receptor of *Hydra*. Glyoxalase requires a tripeptide coenzyme which must be both similar to GSH and contain the free sulphydryl group; for example, asparthione is nearly as effective as GSH[4]. All analogues having the thiol group modified, but retaining the tripeptide structure, are competitive inhibitors (see refs. 5 and 6).

The GSH-receptor of *Hydra*, on the other hand, does not require the thiol group for activity; in this category ophthalmic acid and γ-glutamylalanylglycine[2] and S-methylglutathione (Table 1) are activators. Yet related analogues (ref. 2 and Table 1), having unusually large substituents for the thiol group, do not activate but apparently occupy the receptor site and behave as competitive inhibitors. In contrast to glyoxalase, the GSH-receptor is very sensitive to changes in the glutamyl moiety of GSH, since asparthione does not activate the GSH-receptor but acts as a competitive inhibitor. Furthermore, glutamic acid, while competing with GSH for the GSH-receptor, has no effect on glyoxalase[5].

The part played by the glycyl moiety remains obscure. Glycine alone does not seem to be tightly bound by the receptor as indicated by its failure to act as a competitive inhibitor. None the less, Loomis's demonstration that γ-glutamylcysteine does not activate the receptor[1] indicates that the glycine part of GSH is necessary.

An analysis of the data (Loomis[1], Cliffe and Waley[2], and Table 1) indicates that the GSH-receptor has a most unusual specificity when compared to other proteins reacting with GSH. It is concluded that in order to activate the GSH-receptor, the structure of the tripeptide 'backbone' must be identical to that of GSH, while the thiol group, branching off the 'backbone', can be altered within certain limits.

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Isolation of Chromatographically Pure Rutin from Flowers of Elder

Rutin (3-rhamnoglucoside of 5,7,3',4'-tetrahydroxyflavanol) (I), one of the most widespread flavonoids, has been found in numerous plant materials[1,2]. On the commercial scale for pharmaceutical purposes it is usually manufactured by isolation from stalk and leaves of buck-wheat (*Fagopyrum sagittatum*)[3,4] and from the Japanese pagoda tree (*Sophora japonica*)[3]. A chemically pure preparation is then obtained by repeated recrystallization of the crude product.

(I)

Within the framework of a study of isolation of flavonoid substances from natural material it has been found that chromatographically pure rutin can be easily isolated from flowers of the elder (*Sambucus nigra*). For this purpose chromatographical partition of the extract on powdered polyamide ('Silon') material has been successfully used.

Chromatography on powdered 'Silon' has been used partly for the separation of flavonoid substances from some natural materials[6-8] and partly in their chemical analysis[9].

Dried elder flowers are extracted in a Soxhlet apparatus with 75 per cent methanol so long as the extract is green-yellow coloured. The extract is

then vacuum concentrated and afterwards diluted with water in the ratio of 1 : 1. The resulting sediment of chlorophyll is filtered away, and the filtrate concentrated once more. The extract thus prepared is chromatographically purified on powdered polyamide (granulation 0·1–0·4 mm.). The size of the chromatographical column is dependent on the quantity of the extract. The polyamide powder is first allowed to swell in distilled water for about 1 hr., then the suspension is transferred to the chromatographic column and settled by gentle tapping. The concentrated extract is then passed through the column. Elution is carried out first with water and afterwards with 30 per cent methanol. The water part contains mostly the sugar ballast components; the methanolic fraction the flavonoid substances. The course of elution is watched by means of an ultra-violet lamp, and the fraction showing a brown-green fluorescence is collected. The methanolic eluate is concentrated to a small volume and the resulting sediment of rutin filtered away and dried. By this method it is possible to obtain pure rutin from elder flowers. It has been found that the flowers contain as much as 3 per cent of rutin in the dry residue. The method described makes it possible to recover as much as 90 per cent of rutin which is chromatographically pure.

The melting point of the obtained rutin and the R_F in the solvent system *n*-butanol/acetic acid/water in the ratio 4 : 1 : 2·2 proved to be identical with those of a pure preparation. Acid hydrolysis yields quercetin; from the sugars, glucose and rhamnose in the ratio 1 : 1 have been found. Chemical analysis of the product was also in agreement with pure rutin.

This method of isolating chromatographically pure rutin from elder flowers by partition on powdered polyamide is rapid, simple and easy to carry out. The method is preferable also from the economical point of view, since a chromatographically pure preparation is obtained without any recrystallization.

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Estimation of Volatile Anæsthetics in Tissues by Gas Chromatography

In work on the uptake and elimination of volatile anæsthetics by the body, a convenient method is needed to determine their concentrations in blood, brain, liver, muscle, fat, etc. The elimination of these anæsthetics from the blood follows an exponential law. To determine the elimination curve accurately, a large number of samples has to be taken. It is desirable that the total volume of blood removed be as small as possible, and the method has, therefore, to be as sensitive as possible. This applies particularly to the last part of the curve, when the concentrations of the anæsthetic are low, for example, 10–1 p.p.m.

Conventional methods of estimating di-ethyl ether[1], chloroform and trichloroethylene[2] and halothane[3] are unsatisfactory because they require relatively large samples, lack specificity, and are time-consuming. With these methods concentrations less than 10 p.p.m. are difficult to estimate. Mass or infra-red spectrometry has a sensitivity which is less, that is, about 100 p.p.m. for detection and about 1,000 p.p.m. for estimation.

An elegant solution to the problem is the use of gas chromatography[4]. A method of utilizing the blood sample directly is being developed. At present, however, the anæsthetic is extracted from blood (or other tissue) into *n*-heptane. Using gas chromatography, it is possible to estimate halothane in *n*-heptane at concentrations less than 10 p.p.m.

The separation of *n*-heptane and the anæsthetic is achieved in a column 12 in. long. The column is made of copper refrigeration tubing, ¼ in. internal diameter, packed with 80–100 B.S. mesh 'Celite', which is impregnated with 10 per cent by weight of silicone fluid M.S. 550. The column is maintained at a steady temperature in an air oven. Hydrogen is used as the carrier gas at a flow-rate of about 45 ml./min. Extracts containing more than one substance may require a longer column, perhaps 30 in. long. The temperature of the column should be 25–30° C. for di-ethyl ether and halothane, and for substances with higher boiling points, for example, chloroform, trichloroethylene and methoxyflurane, it should be 100–120° C.

A flame ionization detector modified from that of Harley *et al.*[5] has proved suitable. Gauze electrodes, made of stainless steel, are used on either side of the flame, but not in contact with it. This type of detector appears more sensitive to halogenated compounds than the usual flame detector[6]. A potential difference of 120 V. is placed across the electrodes, and the ionization current is passed through a 1,000 megohm resistor. The resulting potential is measured with a simple balanced cathode follower unit or a vibrating reed electrometer, feeding a potentiometric recorder. Each sample is introduced into the column with a

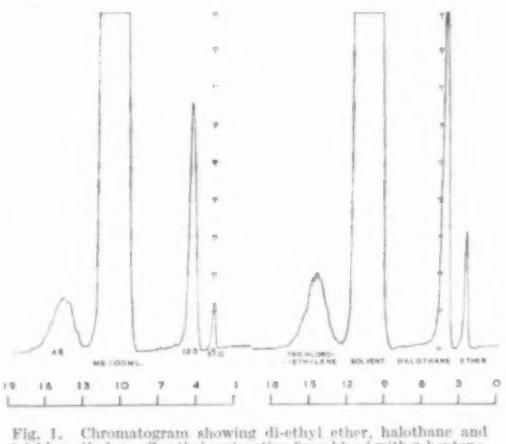

Fig. 1. Chromatogram showing di-ethyl ether, halothane and trichloroethylene after their extraction from blood with *n*-heptane. 'Celite'–silicone column at 30° C.; carrier gas at 45 ml. per min.; 12 in. chart at ½ in. per min. The approximate concentrations are shown beneath the peaks. On the second run (left) the gain was reduced so that the halothane peak could be estimated

capillary pipette[7], delivering 0·15–0·50 μl. The technique for introducing the sample is carefully standardized.

Using this method, halothane can be measured at a concentration of about 10 p.p.m. and a calibration curve had a coefficient of variation of 0·68 per cent. When the peaks on the chromatogram are narrow, their heights rather than their areas may be used for making standard curves. Fig. 1 illustrates the ability of the method to separate and detect different anæsthetics which had been extracted from one sample of blood.

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3-Aminomethylindole and 3-Methylaminomethylindole: New Constituents of Barley

This communication reports the identification of two new alkaloids, related structurally and perhaps biosynthetically to gramine. Shoots of 4-day-old barley seedlings were extracted with trichloracetic acid. The centrifuged solution was extracted with ethyl ether, made alkaline and re-extracted. The ether extract of the alkaline solution was dried and concentrated. Aliquots were chromatographed using paper impregnated with a mixture of 0·2 *M* dipotassium hydrogen phosphate and 0·03 volume of 0·1 *M* citric acid[1] and developed with *iso*propanol equilibrated with 0·29 volume of the same buffer. Sprayed with Millon's reagent[1], the chromatograms showed a strong gramine spot, and two spots called here compounds *A* and *B* and identified by the evidence below as 3-aminomethylindole and 3-methylaminomethylindole respectively. In addition, there was an unidentified spot.

The rate of movement of compound *A* relative to that of gramine ($R_{Gramine}$) is approximately 0·66. It reacts with Millon's reagent to form a yellow-brown spot which gradually acquires a reddish hue, gives a yellow spot with ninhydrin, but no colour with either the benzoquinone or the nitroprusside reagents used to detect secondary amines[2]. Eluted from a paper chromatogram and dissolved in dilute hydrochloric acid, this material displayed a distinctive ultra-violet absorption spectrum in all respects similar to the spectra of authentic 3-aminomethylindole and gramine.

In the presence of compound *A* and of methyl-^{14}C-(−)-S-adenosyl-L-methionine, an enzyme preparation from barley shoots forms a new radioactive compound ($R_{Gramine} = 0·76$). The reaction is dependent on compound *A*. This radioactive compound on treatment with excess methyl iodide in ethanol gives rise to further radioactive spots which were identified chromatographically as gramine and tetramethylammonium salt, and to material(s) which move with an $R_{Gramine}$ of approximately 1·19. These results are entirely compatible with the postulate that compound *A* (3-aminomethylindole) is converted (enzymatically) to 3-methylaminomethylindole. The latter, on treatment with methyl iodide, is changed to gramine, the methyl moiety of which in the presence of methyl iodide is known to be recovered both in tetramethyl-ammonium ion and in other compounds[3].

Authentic 3-aminomethylindole, prepared essentially by Putochin's method[4], displays properties similar to those of compound *A* in all these particulars.

Compound *B* moves with an $R_{Gramine}$ of 0·76, reacts with Millon's reagent to give a final colour intermediate between those of compound *A* and gramine, gives no colour with ninhydrin, but reacts as a secondary amine with the sprays mentioned previously. After elution from a preparative chromatogram, compound *B* has an ultra-violet spectrum in dilute hydrochloric acid similar to that of gramine. Naturally occurring compound *B* is indistinguishable from the compound formed by the enzymatic or (in poor yield) chemical methylation of 3-aminomethylindole. It was further shown that an enzyme obtained from barley shoots forms radioactive gramine when incubated with methyl-^{14}C-(−)-S-adenosyl-L-methionine, this reaction being dependent on the addition of compound *B*.

Taken together, these findings establish the identity of compound *A* with 3-aminomethylindole and of compound *B* with 3-methylaminomethylindole.

Work on the metabolism of these substances is continuing, and will be reported on fully. At present it may be suggested that gramine is formed physiologically by the enzymatic transfer of methyl groups from (−)-S-adenosyl-L-methionine to 3-aminomethylindole to form successively 3-methylaminomethylindole and gramine.

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PHYSIOLOGY

Local Treatment of Experimental Burns with a Monoamine Oxidase Inhibitor

Previous work has shown that prior systemic administration of inhibitors of the enzyme monoamine oxidase led to striking diminution of the increased capillary permeability that followed thermal and chemical injury in rats[1]. Similar anti-inflammatory properties have been reported independently[2]. This effect may be due to the preservation of an adrenaline-like substance the destruction of which by monoamine oxidase might permit the full development of the inflammatory reaction. The present investigation was undertaken to determine whether monamine oxidase inhibitors would reduce inflamma-

tory oedema when applied locally after thermal injury.

Standard thermal injury, in this case 60° for 27 sec., was produced in anæsthetized rats by methods previously published[3]. The monoamine oxidase inhibitor employed was (2-4'-hydroxyphenoxyethyl) hydrazinium chloride (compound 1273, Smith and Nephew Research, Ltd.). The substance was made up as a 5 per cent ointment in a 'Carbowax' base (polyethylene glycol 400, 60 per cent; polyethylene glycol 4,000, 35 per cent). The ointment was applied immediately after completion of the period of thermal injury. It was rubbed in gently but liberally and continuously for 15–20 min., the animals then being returned to their cage. Three hours after thermal injury the rats were killed and the burnt area excised for the assay of inflammatory oedema as described previously[3]. Control rats consisted of untreated animals and of animals treated identically, but with the ointment base alone.

The results were expressed as gm. water/cm.² skin, and are set out in Table 1. In order that the figures given should truly represent inflammatory oedema, the normal water content of skin (0·03 gm./cm.²) was deducted from each set of figures before setting out the table.

Table 1. Effect of Monoamine Oxidase Inhibitor Ointment on Oedema after Standard Thermal Injury

Treatment	No. of animals	Mean value water content of burnt area (gm./cm.²)	Range of values (gm./cm.²)	P
None	12	0·21	0·13–0·35	—
Compound 1273 ointment	10	0·09	0·09–0·10	< 0·001
Ointment base only	6	0·22	0·13–0·35	

It can be seen that thermal injury of this intensity led to a very considerable oedema of skin and subcutaneous tissues. It is equally apparent that application of the ointment containing compound 1273 led to a striking diminution of this increased capillary permeability, whereas similar use of the ointment base alone failed to do so.

It is reasonable to suppose that monoamine oxidase inhibitors have a similar effect when administered locally as an ointment or systemically, that is, by preventing the inactivation of an endogenous adrenaline-like substance the action of which is to diminish capillary permeability to protein[4].

This hypothesis is supported by the inhibition of inflammatory oedema that results from the subcutaneous injection of adrenaline (0·5 mgm./kgm.) up to 30 min. after standard thermal injury (Spector and Willoughby, unpublished observation). On the other hand, intravenous injection of monoamine oxidase inhibitors after thermal injury failed to diminish increased capillary permeability. If ointment and injection operate on similar endogenous mechanisms the discrepancy between their effectiveness after thermal injury must be presumed to be due to better access to the affected tissues by the locally applied substance. Again, if ointment and prior injection work in similar fashion, the present experiments provide further evidence to indicate that, as suggested previously[4], release and destruction of the adrenaline-like substance is a local phenomenon at the site of injury.

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Augmentation of the Pressor Response to Guanethedine by Inhibition of Catechol O-Methyltransferase

Intravenous administration of guanethedine has been reported to cause a pressor response[1,2], contraction of the nictitating membrane of the cat and pilo-erection[2]; the pressor response was not blocked by ganglionic blocking agents[2]. These phenomena lead to the possible conclusion that guanethedine causes a release of catecholamines or has some direct adrenergic effects.

The catecholamines are biochemically inactivated by the enzyme catechol O-methyltransferase[3] and this enzyme is inhibited under both *in vivo* and *in vitro* conditions by various polyphenols[4] which compete with the catecholamines for the enzyme[5]. The results of Wylie *et al.*[6] showed that the effects of both endogenous and exogenous catecholamines could be prolonged by administration of the catechol O-methyltransferase inhibitor pyrogallol; this type of agent, therefore, provides a specific tool for the pharmacological determination of the release of catecholamines.

In the following experiments spinal cats were used, and the blood pressure was determined by cannulation of the carotid artery. In all experiments responses to *l*-adrenaline, *l*-noradrenaline and guanethedine were obtained before and after pyrogallol. The doses of all substances are given as base. The areas of the pressor responses were measured in cm.² by means of a planimeter.

In the first series of experiments on 6 cats the average response to a total of 15 injections of 200 µgm./kgm. of guanethedine was 1·68 ± 0·19 (*S.E.*) cm.². Two min. after administration of 4 mgm./kgm. of pyrogallol to each of the 6 cats, the average response to the standard dose of guanethedine was 5·09 ± 0·26 cm.², and 15 min. later was 3·87 ± 0·19 cm.². The average response to a third injection 32 min. after administration of the pyrogallol was 2·12 ± 0·21 cm.². Thus the pyrogallol markedly augmented the pressor response to guanethedine, and as shown in previous work[4] this action of pyrogallol lasted for about 30 min. In none of these experiments did this dose of guanethedine produce a preliminary hypotension as reported by others[1,2].

Many substances have been reported to release catecholamines from the adrenal glands. In 3 cats the effects of guanethedine alone and immediately following pyrogallol were measured before and after acute bilateral adrenalectomy. In all cats removal of the glands reduced the blood pressure by about 20 mm. mercury; but the responses to guanethedine

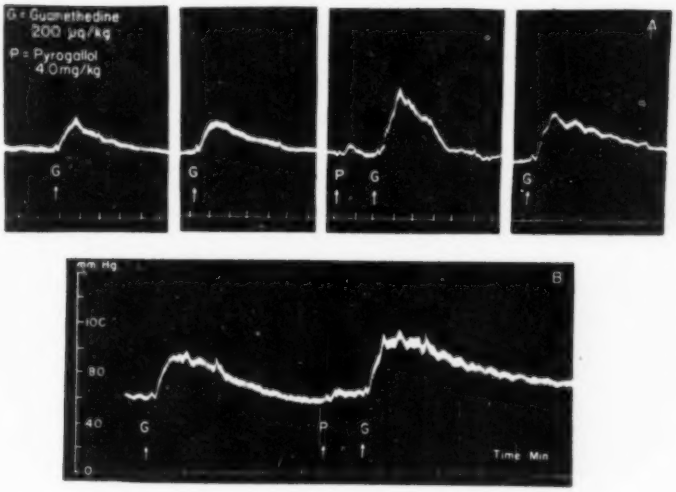

Fig. 1. Pressor responses to guanethedine (*G*) and pyrogallol (*P*) plus guanethedine before and after bilateral adrenalectomy between tracings *A* and *B*

were similar to those before adrenalectomy and could still be augmented by pyrogallol. The tracing obtained during one of these experiments is shown in Fig. 1.

It would therefore appear from the results given here that guanethedine causes a pressor response by the indirect mechanism of releasing catecholamines as this response is augmented by prior administration of pyrogallol, a known catechol O-methyltransferase inhibitor. As the pressor response is not diminished by ganglionic blocking agents[2] and is not much affected by bilateral adrenalectomy, it becomes more probable that guanethedine liberates catecholamines from the sympathetic nerve endings. Such a mechanism of action would explain the sympathetic atony reported by Maxwell *et al.*[3] to follow several hours after medication.

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Rate of Evaporation from Different Regions of the Skin of Indian Zebu Cattle

Indian zebu cattle differ from the cattle of the temperate regions in having a marked hump and voluminous dewlap and navel flap. These structures are specially well developed in areas with very oppressive summer heat, and it has been suggested that these special structures may be related to the animal's greater thermoregulatory power.

The distribution of sweat glands has been studied in the dorsal and ventral skin and in hump, dewlap and navel flap. The secreting surface area of a single sweat gland is not significantly higher in the hump, but the effective secreting surface per sq. cm. of skin surface is much higher owing to a very high concentration of sweat glands[1].

An attempt has been made to study the physiological function or the activity of the sweat glands by determining the evaporation of sweat from different cutaneous surfaces by Berman's method[2]. Cobalt chloride anhydride paper disks (28·3 sq. mm.) were applied on different areas of the body and the time for the complete change of colour noted at an ambient temperature of 38° C. and 74 per cent relative humidity. The average time taken for the dorsal trunk to decolorize the disks was 3 min. 17 sec., and taking this as the standard 100 per cent evaporation, the relative evaporation-rate from other areas was 149 per cent on the hump and 124 per cent on the neck; but the rate on the abdomen was only 72 per cent and on the dewlap and sheath was only 58 per cent. Thus the hump has developed special thermoregulatory significance in the tropical zebu cattle. These findings also confirm the work on the Brahman cattle[3].

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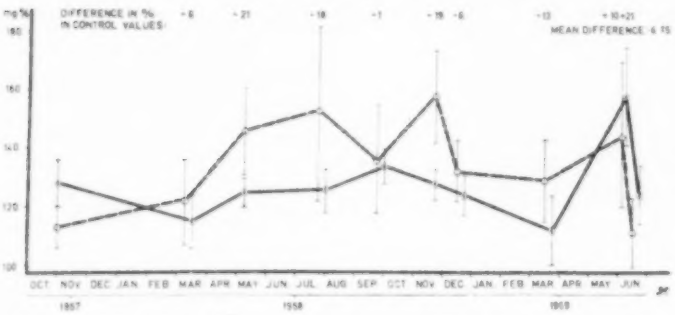
Inability of Refined Corn Oil to influence Spontaneous Arteriosclerosis of Old Hens

According to a large number of reports, vegetable oils (such as corn, cotton-seed, rape-seed, safflower oil, etc.) are able to decrease serum cholesterol both in man and experimental animals. Some evidence exists that this effect is, at least partly, related to the presence of highly unsaturated fatty acids such as linoleic acid. It is not clear, however, whether such vegetable oils also have beneficial effects on arteriosclerotic lesions. After cholesterol-feeding, conflicting results have been reported with rabbits as well as with cockerels. Experimental arteriosclerosis due to cholesterol-feeding may, however, be different from arteriosclerosis in man. Probably the spontaneous arteriosclerotic lesions in old birds, for example hens[1], are more like human arteriosclerosis,

Table 1. Influence of Corn Oil Feeding on Spontaneous Arteriosclerosis in the Aorta of Old Hens (Average ± Mean Error)

Animals receiving*	Macroscopic lesions				Total lipids‡ percentage of:		Total cholesterol§ percentage of:		
	Arcus aortae†	Aorta thor.†	Aorta abd.†	Percentage of total aorta	Fresh weight	Dry weight	Fresh weight	Dry weight	Total lipids
Lard + coconut fat (controls)	1	3 ± 0·6	3 ± 1·7	18 ± 8	3·59 ± 0·17	14·2 ± 1·6	0·38 ± 0·01	1·55 ± 0·13	12·25 ± 6·55
Corn oil	1	2 ± 0·4	2 ± 0·6	15 ± 4	3·81 ± 0·21	14·3 ± 1·5	0·39 ± 0·06	1·62 ± 0·09	11·83 ± 1·96

* See Fig. 1.
† Visual approximation on a 0–6 scale.
‡ The aorta was carefully freed from fat and connective tissue and extracted (ref. 4). The total lipids were purified (ref. 6) and weighed.
§ Liebermann–Burchard reaction with digitonin-precipitable substances of unsaponifiable material.


mg %
DIFFERENCE IN % IN CONTROL VALUES
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OCT NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN FEB MAR APR MAY JUN
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1959

Fig. 1. Influence of dietary corn oil on serum cholesterol (ref. 5) in old arteriosclerotic hens. Points represent average values, vertical lines indicate error. – – –, Controls; ——, corn oil group

We have therefore investigated the effect of dietary corn oil on spontaneous arteriosclerosis of old hens.

Partridge-coloured Italian hens of about two and a half years were fed for 20 months a mash containing 5 per cent corn oil or 5 per cent highly saturated fats respectively. At the beginning of the experiment, randomly selected animals showed fewer aortic lesions than controls at the end of the experiment. Thus the influence of corn oil on existing and progressing arteriosclerosis was investigated.

Diet of controls: 3·0 per cent lard and 2·0 per cent coconut fat (= about 11 per cent of total calories); 6·3 per cent de-skimmed milk powder; 9·3 per cent meat powder; 8·9 per cent yeast; 3·5 per cent hay powder; 24·7 per cent rolled oats; 20·5 per cent wheat grains; 20·8 per cent wheat, rough-ground; 0·9 per cent sodium chloride; 0·1 per cent ferric citrate; 0·01 per cent manganese sulphate.
Number of animals at the end of experiment: 8 (4 animals lost in the course of the experiment because of 'diphtheria', peritonitis, tumour, etc., are not considered). Average body-weight: 1·79 kgm. at the beginning, 2·04 kgm. at the end ($\Delta = +0{\cdot}29$ kgm.).
Diet of corn oil animals: 5·0 per cent corn oil (refined, edible, winterized quality, E. F. Drew and Co., Inc., Bonnton, New Jersey; content of linoleic acid 54·2 per cent, peroxide number 3·85 (analysis by Dr. J. Hofstetter, F. Hoffmann–La Roche and Co., Ltd., Basle) instead of lard and coconut fat.
Number of animals at the end of experiment: 10 (3 lost by similar diseases as controls were not considered). Average body-weight: 1·67 kgm. at the beginning, 2·03 kgm. at the end ($\Delta = +0{\cdot}39$ kgm.).

Fig. 1 shows that dietary corn oil failed to diminish total serum cholesterol. Although in the corn oil group a tendency to decreased levels was obvious, the differences from controls were not significant ($P > 0{\cdot}05$). This finding is in agreement with observations in mature cockerels[2] and growing chicken[3], the serum cholesterol of which was not decreased by oils rich in highly unsaturated fatty acids.

In fowls, the degree of cholesteræmia does not necessarily parallel that of spontaneous arteriosclerosis[4]. Therefore the condition of the arterial tissue itself is of more interest. In the present experiments, however, visible lesions as well as total lipids and cholesterol of the aorta were also not influenced significantly by the corn oil diet ($P > 0{\cdot}05$) (Table I).

Thus, in a long feeding period, 'physiological' amounts of refined edible oil (containing 54 per cent of linoleic acid) failed to diminish spontaneous arteriosclerosis of the aorta in old hens.

The conflicting results with cholesterol-fed rabbits and cockerels, as well as the present negative findings in old hens, do not support the assumption that linoleic acid of vegetable oils has beneficial effects on the development of arteriosclerosis. It remains, however, to be shown whether a higher percentage of corn oil in the diet is needed, or whether hens do not respond like mammals. Before these possibilities are excluded, definite conclusions regarding human arteriosclerosis cannot be drawn.

Addendum. Since submission of this manuscript, it has been reported that even a double amount of corn oil in the diet (10 per cent) fed to Leghorn pullets for the following three years did not affect the development of spontaneous lesions of the abdominal aorta in comparison with controls receiving animal tallow[7].

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Effects of Pulped Soybean Silage on the Milk-yield of Cows

As a result of co-operative investigations carried out with the Research Institute for Animal Physiology, a report has already been published[1] on the summer feeding of green soybeans, in which it was shown that the relative protein-deficiency in green maize silage having a high dry-matter yield may be compensated by the flowering, pod-forming soybean. In the present communication we propose to describe our experimental results on the feeding of silage

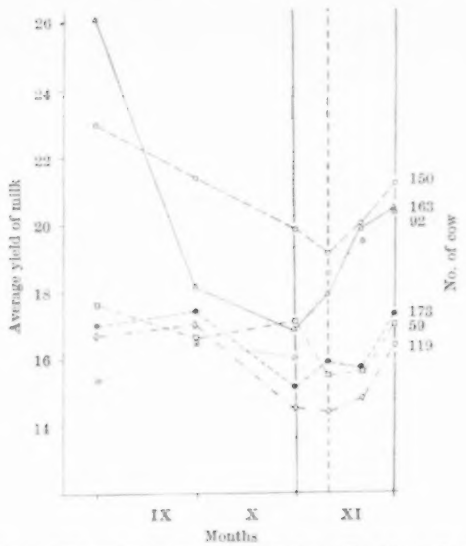

Fig. 1. Milk-production curve during feeding with soybean silage

made from soybeans pulped in the green condition. The analytical results showed that the digestible protein content and starch value of 1 kgm. of wheat bran are equal to the digestible protein content and starch value of 5 kgm. pulped soybean silage. We endeavoured, therefore, to demonstrate in our feeding experiments with pulped soybeans whether from the point of view of food conversion wheat bran can be substituted by soybean-silage.

The wheat bran fed in the preparative and first phase of the experiment was gradually substituted by soybean silage, as shown in Table 1.

Table 1

Experimental phase	Days	Quantity of food fed daily (kgm.)					
		Alfalfa	Best	Chaff	Bran	Maize meal	Soybean silage
Preparative	5	7	15	4	3	12	—
Phase I	5	8	15	3	3	12	—
,, II	5	8	15	3	2	12	5
,, III	5	8	15	3	1	12	10
,, IV	10	8	15	3	—	12	15
Concluding	5	7	15	4	3	12	—

Table 2

Experimental phase	Daily average milk production	Increase in yield in relation to the preparative phase	Relative growth of butterfat (per cent)
Preparative phase	16·2	—	—
Phase I	16·9	0·7	0·1
Phase II	17·3	1·1	0·2
,, III	17·5	1·3	0·2
,, IV	18·8	2·6	0·3

Table 2 shows that there was a considerable increase in the daily average milk production compared with the average shown during the preparative period.

The increased average yield of milk and of its percentage of butterfat contents indicate that soybean-silage is not only a substitute for the wheat bran, but also, due to its stimulating action on milk production, is from the biological and physiological aspects a far more valuable food than wheat bran, although both have the same nutritional value. Indeed, the food conversion value of soybean silage, taking wheat bran as 100 per cent, is 116 per cent. The effect on the lactation curve of feeding soybean silage is illustrated in Fig. 1. We believe that the break in the course of the lactation curve, when it turns upwards, should be interpreted as a hormone effect. Among the large number of physiologically active substances occurring in the soybean only a few may be mentioned the role of which is presumably not negligible: haematin, α-lipoic acid, vitamin E (tocopherol), vitamin K (α-phylloquinone), vitamin B_6 (adermin), pantothenic acid, stigmasterin, sitosterin, campesterin, ergosterin, sapogenol(s), etc. (Karrer[2]). According to Magee and Matrone[3], the œstrogen-like effect of green soybeans stimulates the development of the uterus in mice, and we believe a part is played by the high sterin content of the soybean. The increase of the butterfat content during feeding with soybean silage is equally indicative of the functional activity of acetyl-coenzyme *A* and may perhaps be connected with the relatively high acetyl-coenzyme *A* content of the soybean. It is noteworthy that the relatively high palmitic acid content of soybean oil, and easier linkage of the palmitic acid into the fatty acid cycle, may be, according to Green[4], related to the increased percentage of butterfat during feeding with soybean silage.

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Antiaccelerator Action of Methoxamine

In 1949 it was demonstrated by Otto Krayer[1] that the heart-rate-increasing action of adrenaline could be selectively antagonized by veratramine through a direct inhibitory action on the pacemaker of the heart. Since then it has become established that secondary amine bases of steroid nature among veratrum alkaloids all share this property in common and the term 'anti-accelerator' was given to this property[2]. More recently this property has been recognized as occurring in several types of compounds other than veratrum alkaloids[3,4].

In the course of the systematic investigations of the cardiac action of β-hydroxy-β-(2,5-dimethoxyphenyl)-*iso*propylamine (methoxamine), a synthetic sympathomimetic amine, it was found that in certain concentrations this compound also was capable of antagonizing the cardioaccelerator action of adrenaline, while it produced itself almost no change in the heart-rate. As such a property in a sympathomimetic amine is very interesting because it may provide an important clue to the better understanding of the basic mechanism of the action of the sympathomimetic amines upon the heart, we wish to report the findings briefly. The full account will be published elsewhere in the near future.

The effect can best be demonstrated in the isolated atropinized mammalian heart. We used the heart–

lung preparation of the dog and performed the following two types of experiments.

(1) *Modification of the chronotropic effect of single doses of adrenaline.* When 2–5 μgm. of adrenaline was injected in the heart–lung preparation of the dog, the heart-rate increased considerably to reach a peak in 20 sec. or so and then gradually decreased to the initial level. A second injection proved to be as effective as the first one in its cardioaccelerator action: the same degree of increase in the heart rate occurred and the time course was practically unchanged. However, after administration of 10–20 mgm. of methoxamine, the heart became less sensitive towards the cardioaccelerator action of adrenaline. In a typical experiment administration of 2 μgm. of adrenaline increased the heart-rate from 103 to 157 (increase of 54 per cent). 8 min. after 20 mgm. of methoxamine, the same dose of adrenaline increased the heart-rate from 113 to 121 (increase of only 7 per cent). Later, the effect continued undiminished, and 30 min. after methoxamine the increase in the heart-rate was 118 to 124 (increase of 5 per cent).

(2) *Effect of methoxamine on the cardioaccelerator action of continuous adrenaline infusion.* When adrenaline was administered continuously at a rate of 2–4 μgm. per min. in the heart–lung preparation of the dog, the heart-rate increased gradually to a steady level, its height depending on the rate of administration. Once a steady level was reached, the heart-rate decreased little over a period of as long as 3 hr. When methoxamine was given, in doses of 1·0–100 mgm., to a heart–lung preparation with an augmented heart-rate due to continuous infusion of adrenaline, a decrease in the heart-rate occurred: 1·0 mgm. showed a noticeable, 5 mgm. a marked, decrease; 20 mgm. reduced the acceleration by about 50 per cent and 100 mgm. caused a decrease almost to the initial value (Fig. 1). The steepest fall in the heart-rate occurred during the first 2 or 3 min.: but some further deceleration usually proceeded over a period of subsequent 5–10 min., until a new level was reached. There is a quantitative relationship between the dose of methoxamine and the degree of deceleration. The dose of methoxamine causing 50 per cent inhibition of acceleration was 20 mgm. or thereabouts, a value which makes the anti-accelerator potency of methoxamine approximately one-hundredth of that of veratramine. The nature of this antagonism seems to be competitive, for, even at a time when a certain infusion-rate of adrenaline could no longer increase the heart-rate as the result of inhibitory action of methoxamine, a sufficiently high concentration still was able to give full scope to its characteristic positive chronotropic effect. Thus ten times as much as the initial infusion-rate of adrenaline readily overcame the reduced sensitivity of the heart and led to a very marked increase in the heart-rate (Fig. 1).

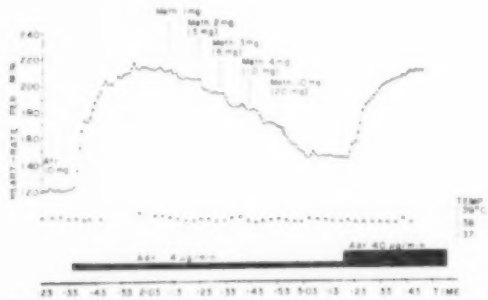

Fig. 1. The graded anti-accelerator effect of methoxamine. Dog, male, 9 kgm. Heart–lung preparation (exp. 11). Mean arterial pressure, 99 mm. mercury. Systemic output, 450 ml./min. Total blood volume at the beginning was about 1,440 ml. Temperature was 38·1 ± 0·3° C. Methoxamine was administered as indicated. The doses in parentheses represent the total amount of methoxamine administered up to the time of the respective signals

Since these actions were observed in the isolated atropinized heart, there is no doubt that they arose from the direct action of this compound on the heart muscle. A recent report from our laboratory has shown that methoxamine reduced the oxygen consumption of the isolated perfused dog heart[5]. Dealing with the protecting action of methoxamine against the toxic effect of X-ray irradiation, Smith *et al.* in their discussion[6] have suggested the reduction of metabolic-rate as the possible cause of the protection. If methoxamine has an inhibitory action on the tissue metabolism as these results imply, such an inhibition of metabolism could be the cause of the above-mentioned antagonism of methoxamine to adrenaline.

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Uptake of Small Resin Particles by the Alimentary Canal of the Calf

The demonstration by Payne, Sansom, Garner, Thomson and Miles[1] that small resin particles can penetrate the wall of the alimentary tract of the calf is clear, but their claim that similar processes may be of nutritional significance is open to doubt.

The highest concentrations of particles detected were in lymph nodes and were all less than $2{\cdot}5 \times 10^3$ c.p.m./10 gm. Even if so high a concentration had been found throughout all the tissues of the animal, the recovery of the radioactivity from an animal weighing 50 kgm. would have been only just a little more than a two-thousandth of the dose administered. As the lymphatic tissue forms a trivial fraction of the body, as muscle, which constitutes about half the body-weight, had approximately one-fiftieth of the activity of the most active lymphatic tissue, and as most other tissues had activities of the order of one-tenth of the maximal lymphatic activity, one may conclude that not more than a thirty-thousandth of the dose lodged in the tissues.

If this represents the fraction traversing the wall of the alimentary tract, such traversal is clearly an improbable event. As such, it may still be important

as a route of infection. But it seems very unlikely that a similar process could be of nutritional significance.

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We are grateful to Prof. R. B. Fisher for his comments but must point out that no claim was made that "similar processes may be of nutritional significance". We presume the sentence under question is: "We suggest that the use of radioactive particles of this kind may prove to be a sensitive method for the study of various problems of infectious disease and possibly also in work on nutrition and nutritional allergy"; but this can scarcely be taken as implying that the absorption of particles is of nutritional significance.

It seemed to us that the demonstration of particulate absorption, however small, might be of interest to those working on the absorption of relatively insoluble elements required in only trace amounts. In this connexion it may be of interest to record that we are endeavouring to determine the relative uptake of particles of different sizes. Experiments of this kind, attempting to measure the 'porosity' of the alimentary canal, may well find some application in work on nutrition although we are mainly interested in the pathogenesis of infectious disease.

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HÆMATOLOGY

Antigenicity of A_2 Hæmoglobin

The heterogeneity of adult human haemoglobin is a well-established fact[1,2]. The present work was designed to determine if the slow electrophoretic fraction A_2 has antigenic specificity and if this fraction can be detected immunologically in cord blood and in the presence of haemoglobin S and C. Previously described[3] techniques were used for the preparation and the agar-gel electrophoresis of the haemolysates. Following electrophoresis the agar gel was cut into sections containing the haemoglobin fractions to be tested for antigenicity. These sections were then frozen, thawed and filtered through fritted Buchner funnels of medium porosity. The short duration (90 min.) and the use of large glass plates as the base of the agar gel made it possible to obtain quantities of eluates sufficient for immunization of rabbits. Eluates of the following fractions were used for this purpose: the main component (A_1) of normal blood and of blood from a patient with thalassaemia minor; the respective A_2 fraction and the non-haemoglobin fraction which we have previously[3] designated 'unidentified component 1' and which probably is identical with Derrien's X_1 fraction[2]. In addition the most cathodic part of the foetal haemoglobin from cord blood (Fig. 1*b*, area between brackets) was eluted from agar gel because of the possibility that this part contains A_2 haemoglobin. Each eluate containing approximately 3 mgm. of protein was combined with an equal volume of Freund's adjuvant and injected into adult male albino rabbits on three or four different sites.

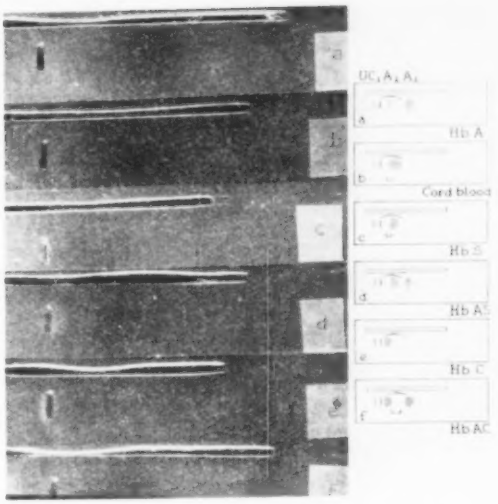

Fig. 1. Immuno-electrophoretic precipitin reaction of A-antiserum and haemolysates. The brackets in *b*, *e*, *f* indicate the areas which were isolated and eluted for immunological studies

Twenty-one days following the injection blood was obtained from the ear artery and this procedure was repeated at weekly intervals. Serum from these samples was tested for antibody content by applying the Ouchterlony agar-gel diffusion technique as modified in this Laboratory[3] and immuno-electrophoresis in agar gel on microscope slides. As test antigens the following material was used: (*a*) agar-gel eluate of the A_1, A_2 and unidentified component 1 fractions of normal and thalassaemic haemoglobin; (*b*) whole haemolysates of normal adult and cord blood and of blood from patients with thalassaemia minor, sickle cell anaemia, sickle cell thalassaemia, A–S and A–C haemoglobin; (*c*) eluates of sections of electrophoretograms of foetal, S, and A–C haemoglobin which correspond to the location of the A_2 fraction (Fig. 1*b*, *e*, *f*, areas between brackets).

Antibody to A_2 haemoglobin appeared three weeks after a single injection of the A_2 fraction. This antibody reacted with haemolysates of normal adult and foetal haemoglobin, haemoglobin S, A–S, A–C (Fig. 1) and S thalassaemia. The precipitation line was always in a position opposite to a place on the electrophoretogram corresponding to the A_2 fraction. On Ouchterlony plates all haemolysates reacted with the antiserum, but when eluates of the isolated fractions were used as test antigens, only A_2, the slowest section of S haemoglobin, and the eluate of the interspace of A and C reacted, which are the areas corresponding to the location of the A_2 component. Antisera to the slowest section of foetal haemoglobin reacted in the same manner as the antiserum to A_2 from thalassaemic and normal blood, suggesting immunological identity of these fractions.

Antibody to A_1 and to unidentified component was demonstrated only following one or two booster injections. A_1 was only weakly, but the unidentified component 1 was strongly, antigenic (Fig. 2). Anti-unidentified component 1 serum cross-reacted slightly with A_2 but not with A_1. A clearly defined precipita-

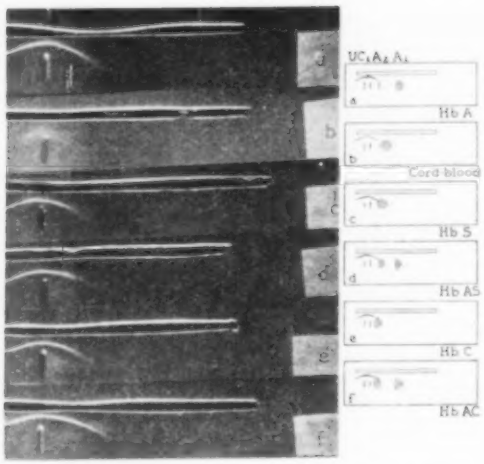

Fig. 2. Immuno-electrophoretic precipitin reaction of the unidentified component 1 antiserum and various hæmolysates

tion line was also present over the unidentified component 1 area in immuno-electrophorotograms of whole hæmolysates of normal adult, fœtal, S, A–S, C and A–C hæmoglobin (Fig. 2). With fœtal hæmoglobin (Fig. 2*b*) this line was not so strong as with the other hæmolysates. Anti-unidentified component 1 antibodies reacted slightly with γ-globulin of serum, but anti-γ-globulin did not react with the unidentified component 1.

It appears from the results of this work that A_2 hæmoglobin has specific antigenicity and that it can be immunologically demonstrated in hæmolysates of fœtal, sickle cell, and C hæmoglobin. Boivin and Hartman[6] recently reported that whole hæmolysates of fœtal, A, S, C and E hæmoglobin share at least two antigenic fractions one of which appears to be the slow component A_2. The present work lends support to this finding by the demonstration of the specific antigenicity of the isolated A_2 fraction. This finding is of interest in view of the recently detected differences in the 'finger print' between A_1 and A_2 hæmoglobin[7].

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Two New Hæmoglobin Variants in a Very Young Human Embryo

In a previous communication[1] we reported the results of a study of the hæmoglobin of 26 human fœtuses and reviewed the relevant literature. In 25 fœtuses from pregnancies of 10 weeks or more we were unable to find a major hæmoglobin component which differed from fœtal hæmoglobin (Hb–F) or adult hæmoglobin (Hb–A). In a 9-week fœtus of 3·5 cm. crown–rump length, however, the largest hæmoglobin component was found to differ from Hb–F and Hb–A; its rate of alkali denaturation was intermediate, as also was its electrophoretic mobility in agar at *p*H 6·2, and it was assumed to be the 'embryonic' hæmoglobin of Drescher and Künzer[2]. The present communication describes the finding of two new hæmoglobin variants in a human fœtus of only 3·4 cm. crown–rump length from a $10\frac{1}{2}$-week pregnancy. For convenience these will be referred to as hæmoglobins Gower 1 and Gower 2.

Approximately 0·2 ml. of blood was obtained immediately after death from the umbilical cord of the intact embryo, following therapeutic termination of pregnancy by hysterotomy, and a hæmoglobin solution prepared from the washed red cells by the method of Singer *et al.*[3]. The behaviour on alkali denaturation and electrophoresis was studied within 24 hr. of the death of the fœtus and the ultra-violet absorption spectrum was analysed later. The results were compared with those obtained on hæmolysates of blood from older fœtuses, full-term new-born infants and adults.

The rate of alkali denaturation studied by the method of Künzer[4] fell within the range given by Drescher and Künzer[2] for cord blood from full-term infants, but outside our own narrower range[1]. The proportion of alkali-resistant hæmoglobin calculated from the rate curve was 56 per cent.

On electrophoresis in agar with citrate buffer *p*H 6·2 (ref. 5) two fractions separated, one migrating similarly to an Hb–F marker and the other to an Hb–A marker.

Electrophoresis on cellulose acetate both with barbiturate buffer *p*H 8·6 and with 0·04 *M* sodium phosphate buffer *p*H 7·7 separated three main fractions plus a very small fast component. The largest fraction corresponded to Hb–F. Hb–A, which can be separated from Hb–F under the particular conditions used with barbiturate buffer, was not detected.

With starch-gel electrophoresis in *tris*-citrate/borate discontinuous buffer[6] three fractions were separated (Fig. 1). The largest corresponded to Hb–F, while the second and third were shown to move more slowly than the Hb–C and Hb–G/C respectively of a hæmolysate containing Hb–A, Hb–G, Hb–C and Hb–G/C (ref. 7). Again no Hb–A appeared to be present.

Direct spectrographic examination of the separated zones in the starch gel was carried out after the gels had been made transparent with glycerol[8]. The tryptophan fine-structure band had the following positions on the fœtal fractions:

Major zone (Hb–F)	2899–2900 Å.
Gower 1 zone	2908 ± 2 Å.
Gower 2 zone	2902 ± 2 Å.

Values obtained for Hb–A and Hb–F zones in control starch-gel analyses of hæmolysates prepared from adults and new-born infants were as follows:

Hb–F	2900 ± 1 Å.
Hb–A	2910 ± 1 Å.

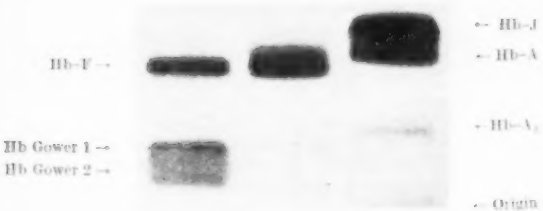

Fig. 1. Starch gel electrophoresis of haemoglobin in the *tris*-citrate/borate discontinuous buffer system (initial gel *p*H 8·8)

The precision of the latter readings was superior as the haemolysates were more concentrated, but the results on the fœtal blood suggest that spectrographically the haemoglobin in the Gower 2 zone is of fœtal type whereas that in the Gower 1 zone resembles Hb–A. It should be noted that the position of the peak of the tryptophan fine-structure band for Hb–F differs from the figure of 2896–7 Å. previously reported[8,9]; this may be due to the presence of non-haem proteins, some of which are known to migrate to the Hb–F position, as well as to background scatter contributed by the gel under the conditions used here. Non-haem proteins may also have influenced the reading in the Gower 2 zone.

The above findings indicate that this embryo carried, in addition to Hb–F, three other haemoglobins. The behaviour of the very minor fraction detected on cellulose acetate suggested that it could be one of the fast-moving haemoglobins occasionally found in some cord bloods[10–12], but this haemoglobin will not be discussed further because the minute amount of the specimen precluded adequate study. Although an appreciable fraction moved to the Hb–A position on agar electrophoresis, it could not in fact have been Hb–A because, by electrophoresis on cellulose acetate at *p*H 8·6 and on starch gel, no Hb–A was detected. Examination of the blood of both parents, who were of Jewish European stock, showed only normal haemoglobin components by starch-gel electrophoresis and less than 2 per cent Hb–F by the 1-min. alkali denaturation procedure[3], so it is extremely unlikely that this fœtus was a carrier of a variant of Hb–A. The Gower 1 and Gower 2 fractions may be presumed, therefore, to represent variants of Hb–F or 'embryonic' haemoglobin. Their behaviour on electrophoresis at alkaline *p*H distinguishes them from all the described Hb–F variants, for Hb–Alexandra[13] which alone moves more slowly than Hb–F differs by migrating faster than Hb–C. Neither can represent the $Hb–F_I$ and $Hb–F_{II}$ fractions separated by chromatography on 'Amberlite *IRC* 50' resin[14], because we have confirmed (authors' unpublished observations) that these column fractions are virtually indistinguishable from Hb–F both electrophoretically and spectrographically[15] and in their rate of alkali denaturation[15,16]. Further precise characterization of the fractions Gower 1 and Gower 2 was not possible, but our results indicate that neither can be as resistant to alkali as Hb–F and that Gower 2 is spectrographically related to Hb–F.

We think it probable that these two new haemoglobins will rarely be seen since we have encountered them only once in the course of examining blood from 32 human fœtuses, and have not found a similar report in the literature. Moreover, we think that it may well be significant that the only two fœtuses in which we have seen haemoglobins other than Hb–F, Hb–A and $Hb–A_2$ had crown–rump measurements of only 3·5 and 3·4 cm., and such small fœtuses are rarely available for study.

We wish to thank Mr. F. Ward for the photograph.

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PATHOLOGY

Tumour-Promotion by Lime Oil in the Mouse Forestomach

In a recent communication[1] it was shown that four different citrus oils promoted tumour development in mouse skin after pretreatment with a sub-carcinogenic dose of 9,10-dimethyl-1,2-benzanthracene (DMBA). Since man is continuously exposed to these oils in his food, it was decided to test one of them, lime oil, both for carcinogenicity and for tumour-promoting activity in the gastro-intestinal tract of mice. Another reason was the hope of demonstrating the two-stage mechanism of carcinogenesis in the alimentary canal. Previous attempts to do this have given inconclusive results[2,3]. In the most recent of these, Berenblum and Haran gave mice a single dose of one of four polycyclic hydrocarbons followed by 3 per cent croton oil weekly for 30 weeks. All treatments were given by stomach tube, and polyethylene glycol 400 (PEG) was the solvent throughout. The appropriate control groups were included. Numerous tumours of the forestomach developed in all their groups, both test and

Table 1. Incidence of Tumours of the Forestomach

Group	Tumour-initiating treatment (a single dose given by stomach tube in 0·25 ml. PEG)	Tumour-promoting treatment (0·05 ml. given by stomach tube once weekly for 40 wk.)	Mice with tumours/ Survivors for 50–280 days*	Tumours > 3 mm. diameter	Total tumours	Average No. of tumours per mouse
I	100 μgm. DMBA	Lime oil	9/9	10	55	6·1
II	100 μgm. DMBA	None	8/10	1	27	2·7
III	200 μgm. 3,4-BP	Lime oil	10/11	8†	38	3·8
IV	200 μgm. 3,4-BP	None	5/11	1	14	1·3
V	50 μgm. 3,4-BP	Lime oil	8/9	3	20	2·2
VI	50 μgm. 3,4-BP	None	0/9	0	0	0
VII	12·5 μgm. 3,4-BP	Lime oil	4/9	2	9	1·0
VIII	12·5 μgm. 3,4-BP	None	2/10	0	2	0·2
IX	Solvent only	Lime oil	3/11	0	4	0·4
X	None	Lime oil	2/8	1	3	0·4
XI	None	None	0/9	0	0	0

* The remaining mice are still under observation.

† One squamous carcinoma invading muscle.

control. It was not stated whether the rest of the intestinal tract was examined. No evidence for tumour-promotion by croton oil was obtained. There are three possible reasons for this: (1) The doses of the hydrocarbons used were too high. Bock and King[4] have since shown that the mouse forestomach is more sensitive than the skin to carcinogenic hydrocarbons. (2) Croton oil, in the concentration used, was carcinogenic. (3) PEG, although a suitable solvent for a single dose of a hydrocarbon[5], reduces the tumour yield when given repeatedly after such a dose[3] and is not, therefore, a suitable solvent for tumour-promoting substances.

In the following experiment some of these difficulties have been overcome; and early results indicate a definite tumour-promoting effect.

Stock female albino mice were randomly divided into 11 groups of 20. Before each treatment the mice were starved for 18 hours. A single dose of DMBA or 3,4-benzpyrene(3,4-BP) in 0·25 ml. of PEG was given by stomach tube, followed, after an interval of 3 weeks, by 40 weekly doses of 0·05 ml. of undiluted lime oil by stomach tube. At this dose-level the mice remained healthy and maintained a steady body weight of 32–35 gm. Mice which died between the fiftieth and the two hundred and eightieth day were examined *postmortem*, and half the survivors at 280 days were killed and similarly examined. Details of treatment and the results are summarized in Table 1.

Tumours of the forestomach were seen in all the groups receiving DMBA or 3,4-BP except group VI, but in the corresponding groups treated with the same doses of DMBA or 3,4-BP, followed by lime oil, many more tumours developed. The difference was most clearly shown in the groups receiving 50 μgm. 3,4-BP. Higher doses of DMBA and 3,4-BP partially obscured this effect. When only the tumours more than 3 mm. in diameter are considered the difference is obvious in all groups: only 2 were seen in the controls, but 22 in the test groups. So far, one malignant tumour has been seen in group III. It was a squamous cell carcinoma, with an area of poorly differentiated cells infiltrating the muscle in several places. In the two groups (IX and X) which received lime oil, but no DMBA or 3,4-BP, 6 tumours were seen including one of 4 mm. diameter. No tumours have been seen in the completely untreated controls, nor in a larger number of untreated mice kept for general observation. It seems that both the hydrocarbons and lime oil possess some oncogenic effect, but the yield of tumours in the groups treated with both agents considerably exceeded the sum of their separate effects. No tumours were seen in the glandular part of the stomach, or elsewhere in the alimentary canal.

These results represent half the experimental mice; the remainder are still under observation, as it is probable that more malignant tumours will develop after 40 weeks, as in similar work on the skin[6].

While the evidence for a two-stage mechanism of carcinogenesis was limited almost entirely to studies on mouse and rabbit skin it was possible to suppose that it was peculiar to the skin and not involved in the genesis of tumours in other tissues. The demonstration of a two-stage process in the mouse forestomach increases the likelihood that it is a general phenomenon. It is true that the epidermis and the epithelium of the forestomach are both of squamous type, but they differ widely in function, in environments to which they are exposed, and in their apparent liability to neoplastic change.

Man is inevitably exposed to small quantities of 3,4-BP and other carcinogens in his environment. Although the amounts may be insufficient to account for carcinogenesis, they are theoretically sufficient for initiation. Recently Roe, Salaman and Cohen[7] have postulated that cigarette smoking acts mainly as a promoter in the induction of human bronchial carcinoma. It is possible that citrus oils act in a similar way in the causation of cancer of the upper alimentary tract. The dose given in this experiment, a total of 2 ml. per mouse during 40 weeks, is approximately equivalent to 4 litres ingested by a man over 30 years, on the basis of comparative body-weight and life-span, and may not be unrealistic. However, it is impossible, at this stage, to extrapolate with any confidence from mouse to man.

I wish to thank Dr. F. J. C. Roe and Dr. M. H. Salaman for their valuable advice throughout this experiment. The expenses of this research were partly defrayed out of a block grant from the British Empire Cancer Campaign.

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Acquired Porphyria in Man and Rat due to Hexachlorobenzene Intoxication

Since 1956, an outbreak of cutaneous porphyria involving several thousand cases has been noted in three south-eastern provinces of Turkey[1]. Affected individuals, predominantly children and adolescents, exhibit photosensitivity with hydroa æstivale, marked porphyrinuria and hepatomegaly, but no abdominal or neurological symptoms. Epidemiological studies suggested the possibility that the disease might be related to the ingestion of wheat treated with a fungicide containing hexachlorobenzene[1,2]. Since direct verification of this possibility by field investigation has not been obtained[1], and since the available toxicological information on hexachlorobenzene is conflicting[3], an attempt was made to produce hexachlorobenzene porphyria in rats.

Adult male Sprague-Dawley rats were fed *ad lib.* ground 'Purina Laboratory Chow' containing 0·2 per cent hexachlorobenzene. Urinary and faecal excretion of porphyrins and porphyrin precursors were determined periodically[4], and tissue porphyrins[5] and liver catalase[6] were measured in rats killed while porphyric.

Of a total of 33 rats started on the experimental diet, 13 died within the first month, exhibiting terminal tremor, ataxia, weakness, and paralysis, without evidence of major disturbance in porphyrin metabolism. In the remaining 20 rats, a significant increase in urinary excretion of porphyrins and porphyrin precursors was first noted after 2 to 8 weeks of hexachlorobenzene administration (Fig. 1). Peak excretory values per 24 hr. were as follows (normal values in parentheses): δ-amino-lævulinic acid, 1·40 mgm. (0·06 mgm.[7]); porphobilinogen, 16·96 mgm. (0·01 mgm.[7]); uroporphyrin, 0·360 mgm. (trace[8]); coproporphyrin, 0·211 mgm. (0·016 mgm.[8]). Slight to moderate increases in fecal excretion of copro- and proto-porphyrin were also noted. From 200 ml. of rat urine, 55 mgm. of crystalline porphobilinogen were obtained[9].

In rats in which hexachlorobenzene administration was discontinued shortly after these peak excretory values had been approximated, the disturbance in porphyrin metabolism was rapidly reversed with return to normal excretion values within a week. However, maintenance of high levels of porphyrin excretion by continued feeding of hexachlorobenzene for two to three weeks resulted in an apparently irreversible porphyric state, in which marked porphyrinuria continued in spite of cessation of drug administration (Fig. 1). These animals died with the neurological complications described above.

Hepatomegaly was common in porphyric rats. Histological studies revealed liver cell degeneration, most prominent around central veins, and increased size and number of Kupffer cells. Chemical analysis of liver tissue showed the following results, per 100 gm. wet tissue (normal values in parentheses): uroporphyrin, 0·4–0·5 mgm. (trace[8]); copro- and proto-porphyrin, 0·05–0·15 mgm. (0·01–0·02 mgm.[8]); porphobilinogen demonstrable[5] in aqueous extract of liver tissue. No significant reduction in liver catalase activity was found.

In the blood, concentrations of hæmoglobin, copro- and proto-porphyrin were normal, while uroporphyrin was not detectable. At autopsy, intense red fluorescence was observed in the cortex of long bones, but not in the marrow.

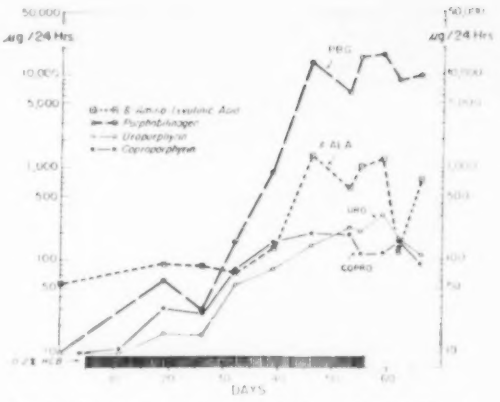

Fig. 1. Urinary excretion of porphyrins and porphyrin precursors in a 350-gm. male rat fed hexachlorobenzene. The rat died on the 68th day of the experiment, that is, 63 days after the start of the hexachlorobenzene administration and 12 days after the toxin had been withdrawn

These results demonstrate that in the rat chronic ingestion of hexachlorobenzene may indeed result in a profound disturbance in porphyrin metabolism, characterized by increased amounts of porphyrins and porphyrin precursors in the liver and excreta, with histological evidence of hepatocellular degeneration. These findings support the suggestion[1], derived on the basis of epidemiological data, that hexachlorobenzene ingestion is the cause of the recent outbreak of porphyria in Turkey. This experimental result is of particular interest in that, hitherto, human porphyria was assumed to be genetically determined, because conclusive evidence for the existence of a purely acquired form of this disease has been lacking. The widespread appearance of porphyria among three genetically distinct populations in south-eastern Turkey—domestic Turks, Kurds and Turks repatriated after several centuries of residence in the Balkans—makes its dependence on an inherited abnormality extremely unlikely.

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RADIOBIOLOGY

Autoradiographical Detection of Tritium-labelled Inulin in the Kidney

By perfusion tests performed on the kidneys of rabbits which had previously been intravenously injected with inulin (100 mgm./kgm. body-weight), it has been shown that inulin was deposited in the kidney tubule cells[1]. These observations were recently confirmed by Balint and Forgacs[2]. Other authors, however, did not agree with my conclusions[3,4].

The autoradiographical detection method seemed suitable to us to obtain further information about the distribution pattern of inulin in the kidney. By means of this technique using tritium-labelled inulin we investigated the kidneys of rats and rabbits.

Alkali-stable inulin was labelled with tritium gas according to the method of Wilzbach[5] (Graul and Hundeshagen[6]). This preparation was dissolved in water and evaporated three times. The final product was obtained by crystallization from an aqueous solution with a mixture of ethanol–ether (v/v, 1/1). Its specific activity was 71·5 μc./mgm. or 286 c./mol. (assumed molecular weight: 4,000), and was alkali-resistant like the initial product. In solution the substance obtained gave a negative reduction test, and after hydrochloric hydrolysis it gave a positive Selivanoff reaction. This is sufficient guarantee that the inulin molecule had not been altered by labelling.

Five mgm. of tritiated inulin was injected under direct vision into the renal artery of an anæsthetized rabbit. After 5 min. the kidneys were removed and fixed in formalin. Transverse sections were examined by the autoradiographical method[6], using an exposure time of 2–9 months. After developing the photochemical layer, the tissue sections were stained with hæmatoxylin–eosin.

Figs. 1 and 2 represent autoradiograms obtained. Over the cells of the proximal and distal tubules there is an obvious blackening, which in other fields appears still more intense, and is even visible in some instances over the tubule lumina.

We obtained corresponding results in rats injected intravenously with tritiated inulin (50 mgm./kgm. body-weight). In these experiments the kidneys were removed after 10 and 20 min. The autoradiograms were not as intensively marked as in the above-mentioned tests, but generally a blackening over the tubule cells was clearly visible.

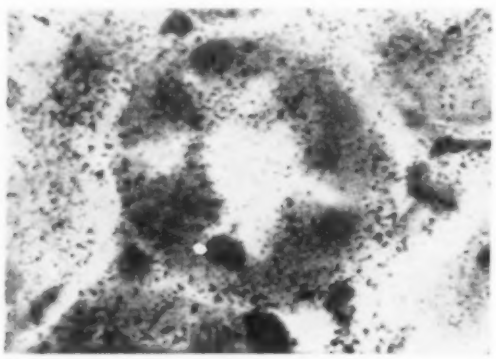

Fig. 1. Autoradiogram of a rabbit kidney 5 min. after injection of 5 mgm. tritiated inulin into the renal artery. Exposure time, 6 months. Proximal tubule. (× *c.* 900)

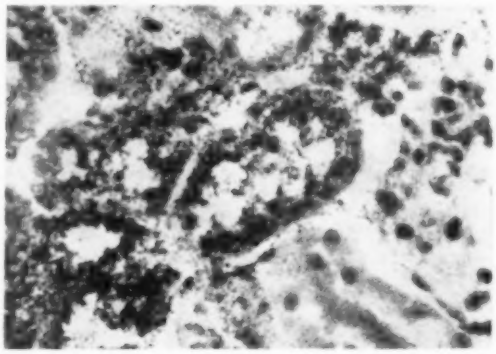

Fig. 2. Experiment similar to Fig. 1. Distal tubule, same as Fig. 1. (× *c.* 360)

The results of these autoradiographical investigations on kidneys with tritiated inulin confirm our opinion that inulin is deposited in the tubule cells of the kidney. No information about the mechanism of this process was obtained.

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Experimental Allergic Encephalomyelitis in Irradiated Rats

Lipton and Freund[1] have produced experimental allergic encephalomyelitis in the rat by intracutaneous injection of homogenized homologous rat brain mixed with paraffin oil and tubercle bacilli. Lumsden[2] reported earlier that in the rat experimental allergic encephalomyelitis can be induced only by injecting the antigen mixture using the intracutaneous and not the subcutaneous route.

If the concept of radiation sickness as an auto-immune disease[3] is valid, then the question may be put whether it would be possible to induce experimental allergic encephalomyelitis in irradiated rats.

In the concept of auto-immune reactions of irradiated animals, which is being reported elsewhere[3], it is necessary to presume that antibody-producing cells undergo a change, that is, they mutate, thus becoming foreign to their own organism. In that manner these cells become antigenically stimulated by the organism's own cells—both normal and those which had also undergone a mutation. Antigenically stimulated cells should be radio-resistant, since immunity already acquired is not impaired by irradiation. By absorbing radiant energy, the antibody-producing cells mutate until they acquire a structure which, according to the clonal selection theory[4],

corresponds to the antigens present in the body. From that moment they should behave as 'already antigenically stimulated cells', that is, they will be radio-resistant and will proliferate.

Experiments were planned so that during irradiation the reinforced brain antigen was already present in the body. The antigen was injected into experimental animals shortly prior to irradiation, with the intention that it should become attached to mutated antibody-producing cells and thus stop their further mutation and direct the immune reaction towards the recipient's own neural tissue.

Twenty albino rats were divided into two groups. The first group, consisting of ten animals, was injected subcutaneously with $2 \times 0{\cdot}25$ ml. per animal of Freund's mixture of homologous rat brain and adjuvant; the second group of ten animals was given $4 \times 0{\cdot}25$ ml. per animal. The amount of tubercle bacilli in the adjuvant was ten times less than prescribed by Freund in order to determine whether irradiation exerts any enhancing effect on the development of the auto-immune process. For the same reason the otherwise inadequate subcutaneous route of injection was used. The injections were given 30 min. prior to X-irradiation. The dose was 600 r. (220 kV., 15 m.amp., 0·5 copper, 1·0 aluminium, r = 40 cm. ~ 120 r./min.). The control group consisted of ten unirradiated animals divided into two groups of five animals each and were injected with the same antigen doses and by the same route.

Results are presented in Table 1. The diagnosis of experimental allergic encephalomyelitis was based on paralysis of limbs and/or marked atactic gait. Eight out of twenty irradiated animals have shown these symptoms, which appeared between the thirteenth and the twentieth day following irradiation. Two belonged to the group which received $2 \times 0{\cdot}25$ ml. of antigen mixture, and six to the group which was given $4 \times 0{\cdot}25$ ml.

Table 1. Incidence of Experimental Allergic Encephalomyelitis (EAE) in Unirradiated and Irradiated Rats following Subcutaneous Injection of Antigen reinforced with Adjuvant

Group of rats	No. of rats	No. of rats which developed symptoms of EAE
Unirradiated	10	0/10
Irradiated	20	8/20

It can be concluded that the inactivity of the immune system following irradiation is only apparent. It is supposed that radiant energy induces mutation of cells which belong to the immune system so that it becomes foreign to its own organism. The mutated antibody-producing cells might react immunologically against any antigen already present in the body and particularly against the antigen reinforced by adjuvant. In order to avoid the objection that the animals were irradiated during the inductive phase, another group consisting of 50 albino rats was injected with the antigen mixture 30 min.–24 hr. following irradiation. The incidence of experimental allergic encephalomyelitis in this group was 19 : 50.

This result favours the concept that the auto-immune processes had already started at the moment of irradiation and that antigen injection had directed it against the recipient's own neural tissue. Although this result requires further investigations, it does not invalidate essentially the concept of the auto-immune process as a cause of radiation sickness.

The beneficial effect of isologous bone marrow in the treatment of irradiation sickness might represent a serious objection to the concept of irradiation sickness as auto-immune disease. It should, however, be kept in mind that by injection of bone marrow we carry into the irradiated animal normal cells capable of antibody production.

The possibility that increased permeability of cells caused by irradiation might accelerate the contact of antigen with antibody-producing cells would mean that histamine or serotonin injection should enhance the auto-immune reaction. However, these two compounds are potent protectors against radiation damage.

Analogous experiments using other organs as antigen and changing dose and time of injection and dose of irradiation should elucidate this phenomenon and check the validity of the concept.

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Distribution of Phenyl Mercuric Chloride labelled with Mercury-203, applied as a Seed Dressing, in the Tissues of the Young Carnation Plant

Organo-mercury compounds are good fungicides; they are applied to oat seeds to control *Helminthosporium* infection[1], to *Narcissus* bulbs to control *Fusarium oxysporum*[2] rot and to gladiolus corms to prevent disease caused by *Sclerotium gladioli*[3]. However, the mercury compound may damage the plant; growth of oat seedlings is less than normal when phenyl mercuric acetate is applied to the soil to protect seed[4]. Experiments described here illustrate the way in which damage to seedlings may occur when phenyl mercuric chloride is used as seed dressing to control rot in carnation seedlings.

Seeds of Annual Charm carnations were treated with varying amounts of phenyl mercuric chloride labelled with mercury-203 as follows. Groups of twenty seeds were placed in Petri dishes on wire gauze supports over a solution of phenyl mercuric chloride in dioxan (2 mgm./ml.). Control groups were exposed to dioxan vapour only or left in the dishes in the same place as experimental seeds. The amounts of dressing on the seeds were varied thus: (*a*) by exposing seeds to the vapour from the phenyl mercuric chloride solution for 24 hr. at 18° C. (Exp. 1); (*b*) by exposing them for 2–3 days at 37° C. (Exps. 2, 3); (*c*) by dipping them in the dressing solution and drying with filter paper (Exp. 4). The amount of phenyl mercuric chloride on the seeds was measured in a well-type gamma-scintillation counter which had an efficiency of *c.* 34 per cent for mercury-203. The seeds were sown in crystallizing dishes containing sterilized vermiculite, horticultural grade. They were watered with a solution containing 5 gm. urea, 5 gm. potassium dihydrogen phosphate, 2 gm. magnesium sulphate, 1 gm. ferrous sulphate and traces of manganese sulphate, calcium chloride, boric acid

Fig. 1. Top, Exp. No. 2. Left, 8-week-old seedlings; right, autoradiograph of the seedlings to show the distribution of phenyl mercuric chloride labelled with mercury-203. Bottom, Exp. No. 3. Left, 7-week-old seedlings; right, autoradiograph to show the distribution of the labelled phenyl mercuric chloride

and sodium molybdate dissolved in 1 gal. water. The dishes were covered with polythene sheets and placed in 30° C. incubator until germination occurred. After about 3–4 weeks the seedlings were transplanted into larger enamel trays containing vermiculite and nutrient solution. The testas from germinated seeds and 4 young plants from each experiment were counted. Results are tabulated in Table 1.

The treated seedlings from Exps. 1 and 2 grew well, but in 1, one seedling had mottled cotyledons, and in 2, three seedlings had this appearance. In Exp. 3, four seedlings died early. All these failed to develop a normal root and one had mottled cotyledons. None of the control plants had damaged roots or cotyledons. In Exp. 4 the seeds received a dose of β-radiation in the range of 17–22 rads when they took 7 days to germinate. This is probably insufficient to reduce germination, since a dose of $3{\cdot}6 \times 10^3$ rads is necessary to reduce the germination of very radiosensitive seeds of *Pinus sylvestris* by 50 per cent (H. J. Bowen, private communication). However, when the seeds were treated with inactive phenyl mercuric chloride so that approximately 200 μgm. of material was deposited on the seed, germination was completely inhibited.

Young plants from experiments 1–3 aged eight or nine weeks were taken from vermiculite media washed to free the roots from particles, dried and pressed on to 'Cellophane'. They were then exposed to 'Ilfox–X-ray' film for 4–6 weeks and the film developed normally.

Fig. 1 shows the distribution of radioactivity in the plant. Phenyl mercuric chloride has concentrated strongly in the cotyledon leaves, hypocotyl and root adjacent to the hypocotyl. These plant organs appeared to be damaged in some plants in the experiments described. Some seed leaves contained phenyl mercuric chloride but were not mottled, and only a proportion of the roots which contained the compound were damaged.

An experiment was made to discover whether the smallest amount (1·92 μgm.) of phenyl mercuric chloride on the seed would prevent an infection of Dianthus seeds caused by *Trichothecium*. Seeds which had small fungal colonies on the testa were placed over phenylmercuric chloride in dioxan (2 mgm./ml.) for 24 hr. at room temperature. This treatment was the same as that in Exp. 1, which resulted in 1·92 μgm. of labelled phenyl mercuric chloride being deposited on the seed. Thirty treated seeds and untreated seeds were placed on moist tissue paper to germinate. After four days the untreated seeds were covered with mould and all failed to germinate. 75 per cent of the treated seeds germinated; only one showed mould, which was a species of *Penicillium*.

One of us (P. F.) has observed damage similar to that caused by phenyl mercuric chloride to the seedlings of carnations when seed was treated with 'Vegetable Seed Saver'. The cotyledon leaves were spotted with areas of dead tissue and growth was retarded. Occasionally seedlings failed to grow at all because no root developed. 'Vegetable Seed Saver' contains the fungicide tetra methyl thiuram disulphide (thiram). The damage caused by this and phenyl mercuric chloride is very similar with this strain of carnation.

Phenyl mercuric chloride has a strong affinity for the sulphydryl groups of protein[5]. The above results suggest that phenyl mercuric chloride has combined with protein substances in the cotyledons, hypocotyl and root, organs which are recognizable in the seed. The mercury protein was transferred from the hypocotyl to the root, but the amount in the root tip was less than that in the region nearest the hypocotyl (Fig. 1). This distribution could be explained by assuming that the mercury-protein is transferred passively during cell division and that new protein is being actively synthesized in the region of the root tip. The new protein would dilute the mercury-protein present in the dividing cell. The —SH-containing protein necessary for root growth could be derived initially from S—S protein in the cotyledons and later by synthesis from sulphate present in the growth medium. No transfer of mercury protein to the stem apex or leaves occurs although large amounts are present in the cotyledons; the reason for this is not apparent.

The similarities between the damage caused by phenyl mercuric chloride and tetra methyl thiuram disulphide may be the result of coupling with the same sulphydryl-containing compounds. Certain

Table 1

Amount of activity, counts/min.		Weight (av.) of phenyl mercuric chloride/seed (μgm.)	Testa counts/min. (av.)	Seedling counts/min. (av.)	No. of seedlings appeared	
Exp. No.	Av./seed				Treated with phenyl mercuric chloride	Dioxan control
1	978	1·92	236	284	15	16
2	1,997	3·9	330	244	13	11
3	3,663	7·23	502	1,144	14	11
4	95,050	186·6	no germination		(4 died) —	13

In Exp. 1, 17 out of 20 untreated seeds germinated.

disulphides are known to couple selectively with —SH-containing compounds. However, a more direct comparison of the action of these fungicides on plant tissue could be made if thiram was labelled with sulphur-35. The experiments do indicate that phenyl mercuric chloride applied at the rate of 2 μgm./seed is an effective fungicide. In amounts greater than 4 μgm./seed the seedlings will be damaged, probably owing to the reduction in the quantity of SH-protein in the root and cotyledon tissues.

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BIOLOGY

Species-characterizing Antigens of 'L' and 'ERK' Cells

CELL culture has become a very important procedure in both biological and medical research, and with the many continuous lines of cells available to-day it is necessary to have methods to check the identity of any given culture of cells.

With proper attention to the special needs of the problem, there must be many immunological methods that could be adapted for this purpose. Recently, we[1] have reported on the use of the mixed agglutination reaction for the recognition of the species of origin of cells in culture. In this communication we wish to report briefly our findings on two continuous lines of cells, namely, the 'L' and 'ERK' strains, using the mixed agglutination reaction and antisera apparently specific for tissue cells of the various animal species.

The histories of these two strains are as follows. The 'L' strain[2] is of mouse origin, the parent strain having been derived in 1940 from the subcutaneous and adipose tissue of a 100-day-old male mouse of the *C3H* strain Andervont sub-strain. One group of cultures from this parent strain was treated with 3-methylcholanthrene at a concentration of 2·0–2·5 μgm./ml. for 111 days, and was designated strain 'L'. The parent strain prior to this treatment was grown on a fowl plasma–embryo extract clot, with a supernatant fluid medium consisting of Earle's saline (40 per cent), horse serum (40 per cent) and fowl embryo extract (20 per cent); strain 'L' cells were cultured initially in the same way, and have since been grown as monolayers on glass under the same fluid medium for some years. The cells used here were derived from a sample provided by Dr. J. Paul, and have been grown as monolayers on glass in Eagle's medium supplemented with 10 per cent bovine serum.

The 'ERK/1' strain was derived by trypsinization of one kidney of an embryonic rabbit by Westwood *et al.*[3]; it was cultured initially on glass in roller bottles in a medium consisting of rabbit serum (10 per cent), 'TPY' supplement (5 per cent), cysteine-hydrochloride (0·02 per cent) and Earle's saline (to

Table 1. MIXED AGGLUTINATION TESTS ON 'L' AND 'ERK' CELLS TO REVEAL THEIR SPECIES-CHARACTERIZING ANTIGENS

Red cell antisera rendered specific for recognition of species antigens on tissue cells	Indicator red cells	Cells growing in culture										
		Under test 'L' strain[1]	Control panel									Under test 'ERK'[11] strain
			Mouse[2]	Rat[3]	Bovine[4]	Pig[5]	Guinea[6] pig	Rabbit[7]	Rhesus[8] monkey	Human[9] *KB* strain	Human[10] HeLa strain	
Rabbit anti-human red cell[12]	Human group O	0	0		0	0	0	0	20	**160**	**160**	160
Guinea pig anti-rabbit red cell[12]	Rabbit[12]	0	0	0	0	0	0	**80**	0	0	0	0
Rabbit anti-pig red cell[14]	Pig group O	0	0	0	0	**20**		0			0	0
Rabbit anti-bovine red cell[13]	Bovine[13]	0	0	0	**640**	0	0	0	0	0	0	0
Rabbit anti-mouse red cell[13]	Mouse	320	**320**	80	0	0		0	0	*	0*	0*

Figures in columns indicate titres of serum giving mixed agglutination. Where no figures are shown no test was performed. Homologous reaction in bold type.

[1] Cultured, from sample provided by Dr. J. Paul, in Eagle's medium supplemented with 10 per cent bovine serum.
[2] Isolated by tryptic digestion from new-born mouse skin; cultured in medium 199 supplemented with 20 per cent mouse serum.
[3] Isolated by tryptic digestion from foetal rat skin; cultured in medium 199 supplemented with 20 per cent rat serum.
[4] Isolated by tryptic digestion from adult bovine kidney; cultured in mixture of 79 per cent Hanks's solution, 20 per cent bovine serum, 1 per cent lactalbumin hydrolysate in P.B.S.
[5] Isolated by tryptic digestion from adult pig kidney; cultured in mixture of 79 per cent Hanks's solution, 20 per cent pig serum, 1 per cent lactalbumin hydrolysate in P.B.S.
[6] Isolated by tryptic digestion from adult guinea pig kidney; cultured in medium 199 supplemented with 20 per cent guinea pig serum.
[7] Isolated by tryptic digestion from adult rabbit kidney; cultured in medium 199 supplemented with 20 per cent rabbit serum.
[8] Isolated by tryptic digestion from adult rhesus monkey kidney; cultured in medium 199 supplemented with 0·14 per cent bovine albumin and 0·1 per cent peptone.
[9] Derived from a sample obtained from the Research Institute (Animal Virus Diseases), Pirbright; cultured in Eagle's medium supplemented with 10 per cent bovine serum.
[10] Derived from a sample obtained from the Institute for Medical Research, Mill Hill; cultured in Eagle's medium supplemented with 10 per cent bovine serum.
[11] A sample obtained direct from Dr. J. C. N. Westwood (cultured in Earle's medium supplemented with 15 per cent calf serum).
[12] Red cells treated with papain before being used in the tests.
[13] 1 : 10 most concentrated dilution of serum tested.
[14] 1 : 5 most concentrated dilution of serum tested.

* Occasionally slight affinity between cultured cells (untreated with specific antiserum) and mouse red cells—a phenomenon that is being investigated.

100 per cent) ('TPY': Tryptic meat broth, 88 per cent; peptic digest of sheep's blood, 2 per cent; yeast extract, 10 per cent). Epithelial cells grew out first, but were later replaced by fibroblasts, which persisted until the seventh passage. At this time most of the cells degenerated, and the cultures were kept for 17 days without a change of medium. A plaque of epithelial cells was then noted in one bottle, and from this plaque the strain 'ERK/1' was easily developed. The sample of 'ERK/1' cells used here was provided by Dr. J. C. N. Westwood and had been cultured in Earle's medium supplemented with 15 per cent calf serum.

The mixed agglutination reaction was developed by Coombs *et al.*[4] for the purpose, originally, of demonstrating blood group antigens on tissue cells. The reaction involves the formation of mixed clumps (which are easy to observe under a phase-contrast microscope) between tissue cells and indicator red cells if the two cell types possess a common antigen.

The adaptation of the method to the problem of recognizing the species-antigenic characteristics of cells growing in culture depends on the assumption, upheld empirically[1], that red blood cells and other tissue cells of the body, or such cells in culture, possess in common certain antigens characterizing the species. In the tests made so far, anti-red cell sera have been used and have been absorbed with tissue cells and red cells of various heterologous species to render them species-specific in their reaction[1]. In essence the reaction is performed as follows. The suspension of cultured cells under investigation is treated in separate tests with the diagnostic red cell antisera, and after being washed free of uncombined antibody is added to a suspension of homologous red cells. An affinity between the antibody-treated tissue cells and the red cells, manifested by the formation of mixed agglutination, indicates common antigenic structures and by implication the species nature of the test cell.

Subjecting 'L' and 'ERK' cells, together with a large panel of cultured cells of known origin as controls, to such an examination gave the results shown in Table 1; relevant details about each cell culture are given in a footnote to Table 1.

The specificity of the diagnostic sera used may be seen from the results of the tests on the control panel of cultured cells. There seems to be no doubt that 'L' cells are still mouse in antigenic character, since they reacted strongly with the anti-mouse serum and not at all with the sera diagnostic for the human or bovine species or that of the rabbit and pig. On the other hand, the 'ERK' cells failed to give a positive reaction with the anti-rabbit serum but reacted strongly with the anti-human serum only. The most obvious conclusion is that the 'ERK' cell is a human cell.

Other characterizing antigens may be used in such mixed agglutination tests on cultured cells besides these rather ill-defined 'species antigens'. Tests for human *iso*antigens have already been reported on HeLa cells[5], and our findings will soon be published on the use of 'heterophile' antibodies establishing the presence of antigens of the Forssman type.

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Nucleic Acids as Transplantation Antigens

Much has been written about the role of nucleic acids in transplantation immunity[1–3]. From previous work it has been concluded that deoxyribonucleic acid (DNA) was not antigenic. The following results, based on chemical analysis including chromatography of sugars[4] and of purines and pyrimidines or their derivatives, suggest that ribonucleic acid (RNA) also is not a necessary part of the antigenic molecule. Antigens from mouse spleen and thymus were prepared by different procedures[5–7]. Their antigenicity was checked by techniques previously described[3].

Antigen I has been prepared by precipitation at *p*H 5 (Table 1). Accordingly, its RNA content was high. By incubation with trypsin, 60–80 per cent of this material was solubilized. The sediment (preparation II) kept the major part of the antigenic activity, its RNA content was considerably lowered, while its percentage in galactose + mannose was increased. Further treatment of this sediment by ribonuclease led to the removal of any detectable trace of RNA without any loss of activity (preparation III). By this treatment no change in the hexose content was found.

It must be emphasized that preparation I, not previously treated by trypsin, was resistant to ribonuclease, the RNA fraction being most probably surrounded by a protective proteic layer. The constant hexose content at about 3–4 per cent, coupled with a percentage of hexosamine to proteins at 1–2

Table 1. Composition in Percentage of some Transplantation Antigens extracted by Different Procedures

	Injected dose (mgm. of proteins)*	Proteins	DNA	RNA	Galactose + mannose
I (ref.5)	1·5	83·3	1·1	13·9	1·7
II†	0·5	92·6	3	2·48	4·9
III‡	0·5	96		0	4
IV§ (ref.6)	0·22	93·5	2·5	1·5	2·5
V	1·1	67·1	29·3	1·5	3
VI	0·15	85·1		11·8	3·1

* Usually equivalent to 500×10^6 cells; preparation V from 5×10^6 cells.
† Sediment after centrifuging 30 min. at 25,000*g* the trypsin-treated preparation I.
‡ Sediment after centrifuging 20 min. at 25,000*g* the ribonuclease-treated preparation II.
§ Kindly supplied by Dr. G. Lejeune.

per cent, suggests that the antigenic determinant could be carried by a glycoprotein. It must be added that the presence of fucose is suspected but could not be confirmed. Rhamnose was never found. Table 1 includes the analysis of other preparations obtained by different procedures. Preparation IV [6] is, in part, based on the action of trypsin. Its composition is very near that of preparation II. Preparation V is that of Billingham, Brent and Medawar[7]; it is very rich in DNA, but its hexose content is very similar to that of previous preparations. Preparation VI [8] has been obtained by electrophoretic separation.

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Electron Microscopic Autoradiography in a Magnetic Field

THE feasibility of electron microscopic autoradiography was suggested to us by the report of O'Brien and George[1]. We have tried a similar technique with tritiated thymidine in tissue culture and have found that recognition of reacted grains in the nuclear track emulsion may be greatly facilitated by their distinctive filamentous appearance, and that the intensity of labelling may be increased by exposing the grids in a strong magnetic field.

HeLa cells were grown in a medium containing tritiated thymidine, and standard techniques were used to prepare thin sections of the cells for electron microscopy. A small amount of Kodak nuclear track emulsion *NTB3* was liquefied by heating in a water-bath at 45° C. and was diluted with 2 parts of water. After stirring, the diluted emulsion was allowed to stand for 20 min. at room temperature to eliminate bubbles. Sections mounted on stainless steel grids were touched to drops of the diluted emulsion, and the excess emulsion was drained away by touching the edges of the grids to filter paper. After exposure in the dark for several weeks and developing with *D19* developer, examination in the electron microscope showed filamentous spots over the nuclei of cells (Fig. 1). Such spots were shown to be the result of radioactivity by controls in which the sections of cells were omitted and the tritiated compound was mixed with the emulsion. That the spots consisted of reacted grains in the emulsion was demonstrated when no radioactive substance was present and the grids were exposed to light.

Some reacted grains were visualized outside the nuclear membrane, and we sought to eliminate this scatter by exposure of the emulsion-covered grids to a magnetic field. The use of a magnetic field was suggested by Dr. M. Ter Pogossian, who calculated that the low-energy electrons of tritium would be affected by a flux density of 10 kilogauss and who was able to supply a magnet of this intensity. The result did not show complete elimination of scatter, and it was difficult to make any quantitative estimation of the amount of scatter. However, it was found that the reacted grains over nuclei in preparations exposed to the magnetic field were considerably more numerous than in preparations not exposed (Figs. 2 and 3).

It appears that the distinctive contour of the filamentous spots and the increased intensity of labelling brought about by the magnetic field are technical aids which may help to combine the advantages of tritium autoradiography with the resolving power of the electron microscope. The filamentous shape of the reacted grains may be used to distinguish them from other spots and from arte-

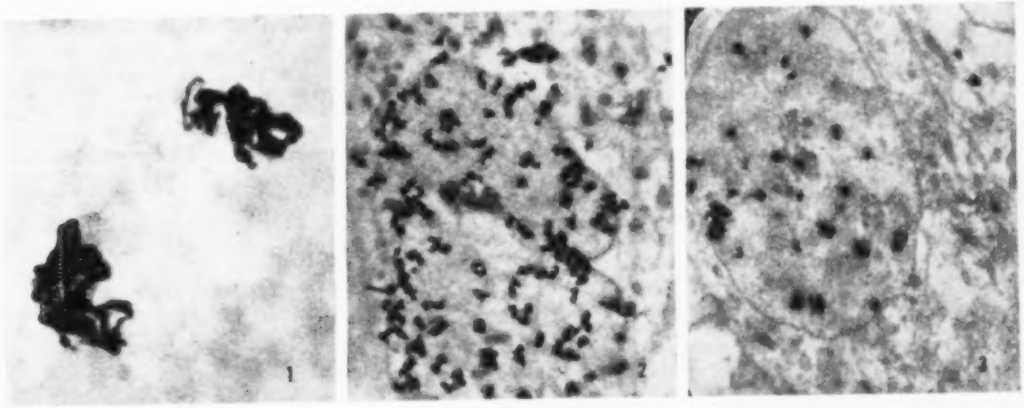

Fig. 1. Filamentous contour of reacted grains over the nucleus of a HeLa cell. The nuclear track emulsion was exposed to the section for 8 days. (× 37,500)

Fig. 2. Reacted grains over the nucleus of a cell after exposure of the emulsion to the section for 32 days in a magnetic field. (× 3,500)

Fig. 3. Control emulsion exposed to the section for 35 days without a magnetic field. (× 3,500)
Cells were grown for 2 days in the medium containing tritiated thymidine (3·3 μc. per ml. of medium, specific activity 890 mc. per m.mole)
Sections for Figs. 2 and 3 were cut from the same block and were slightly thicker than those usually used for electron microscopy

facts that may be seen in electron micrographs. The increased numbers of reacted grains after exposure of emulsion-covered grids to a magnetic field may serve to shorten the times needed for exposure and reduce the amount of radioactivity needed in thin sections to obtain satisfactory electron autoradiographs.

A more detailed account of this work will be published in *Laboratory Investigation*.

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Status of the Grey Seal

The leading article in *Nature* on "The Grey Seal and British Fisheries"[1], by relying on Rae's[2] appendix, gives a wrong impression of our knowledge of the status of the grey seal (*Halichoerus grypus*) in British waters both now and in the past. There has in fact at no time been adequate information on which to base a reliable estimate of the total population of this species. Added to this ignorance there has been, and still remains, much confusion with the common seal (*Phoca vitulina*), and the recent work of several zoologists on the biology of the grey seal has resulted in the discovery of previously unknown breeding groups which are not necessarily new colonies. An increase in knowledge of a species does not mean that there has been an increase in its numbers.

Without direct total or sample counts neither absolute nor comparative populations can be estimated except by recourse to indirect methods. The biology of the grey seal creates difficulties at all stages; for example, although the breeding season extends for about three months, the breeding cows are present only for two to three weeks, so that on no one day can they all be counted together; some have departed before others arrive. The same applies to the pups, although they are present on the average for 4–5 weeks. The number of breeding bulls is much smaller, possibly as little as one-tenth that of the cows. Does this represent all the bulls of comparable ages with the cows, or are the others alive but at sea? Again the non-breeding individuals are conspicuous by their absence[3–5]. They must be at sea or in some unknown proportion hauled out on rocks which are not used for breeding.

At other times of the year the grey seals are distributed over fairly wide areas of the seas around the coasts of Britain, as marking investigations have shown. No counts are possible under these conditions.

To make a reasonable estimate of the population, it is therefore necessary to have some idea of a life-table. Davies[6] attempted this, but, where no information was available, had to make assumptions such as the age of puberty in both cows and bulls, and the potential longevity. Annual mortality-rates were taken from Kenyon and Scheffer for the northern fur-seal. Since Hewer[7] has shown how to determine the age of a grey seal, we now know that Davies's assumptions were incorrect. The cows do not live for twelve years but for more than thirty. They do not have their first pup when two years old but when about six. Such knowledge materially affects any calculation of population numbers. The position of the bulls is still obscure; but I am informed that there may well be fewer than half as many bulls as cows in any colony, taking non-breeding and breeding individuals together. This alone would reduce the estimated population by 25 per cent.

The moral of this surely is that we should forget all previous guesses and figures since they cannot do more than lead us astray. Instead of arguing on the basis of valueless data, our efforts should be directed towards getting the data needed for reasonably sound estimates.

Meanwhile it should be remembered that even if the total number of grey seals is two or three times as great as the wildest estimate so far made, it would still be a comparatively rare seal on a world scale. The Norwegian catch of young harp and bearded seals combined (which is less than 50 per cent of the total catch) is about 300,000 per annum in recent years. Such figures could only be maintained on populations vastly in excess of that of the grey seal.

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Root-knot Nematodes and Legume Nodules

Published descriptions of the course of infestation of roots of legume species by root-knot nematodes (*Meloidogyne* spp.) are not new. As early as 1932 Godfrey and Oliveira[1] followed the process of infestation in cowpea (*Vigna sinensis*) in root observation boxes containing sterilized soil.

In the Leguminosae, where the phenomenon of symbiotic nitrogen fixation is so significant, little appears to have been done in investigating the interrelationships between *Rhizobium* spp., root-knot nematodes and their leguminous hosts, either under experimental or natural conditions. There is a mere mention by Van Schreven[2] and Masefield[3] regarding the possible role of the nematodes in modifying nodulation and nitrogen assimilation. Christie[4] reported finding root-knot nematodes in the nodules of soybean plants that were otherwise apparently free from nematode galls.

Fig. 1. Morphological difference between mature nematode-free nodules (*r*) and the gall-like structures (*n*) which may be either transformed nodules or true nematode galls, as found on velvet bean (*Stizolobium* sp.)

Recent field and laboratory observations of the root systems of the cowpea-legume group (*Vigna sinensis* var. and *Stizolobium* spp.) grown in sub-tropical and tropical locations of the sugar cane belt in Australia show that: (1) the infestation of nodules (and other root sites) of the above legumes by the root-knot nematode, *Meloidogyne javanica* (Treub) Chitwood, is a common occurrence in these localities; (2) on certain plants the nodules only may be attacked; (3) throughout one growth-cycle a large percentage of nodules may become infested; solitary nodules in lower root zones will often escape infestation; (4) nodules reach various sizes before initial infestation though smaller (younger?) nodules appear more susceptible.

The finding of nodules in all intermediate stages from those exhibiting larval penetration only (together with a preponderance of *Rhizobium*-occupied tissue) to those in which multiple or secondary infestation (but no bacteria) predominates suggests that the production of nodule or gall depends on the subsequent development of the early nodule after attack by the eelworm (Fig. 1). It is not yet known whether nodules can resist or recover from nematode infestation, and answers to these questions are being sought from present work under controlled conditions.

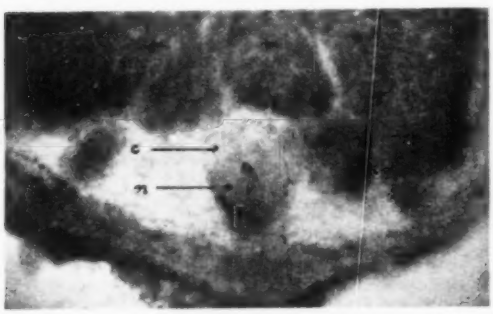

Fig. 2. Transverse section through a nodule from velvet bean showing (*r*) inner tissue containing *Rhizobium*-filled cells, (*n*) sessile female *Meloidogyne* developing in the outer cortex, behind which the outlines of giant multinucleate cells may be seen (*c*). (× *c*. 56)

One interesting feature of the secondary infestation of the nodule by the nematode is that giant cells develop on which the swollen female nematode feeds, as in the case when plant roots are carrying true nematode galls (Fig. 2). This raises the intriguing speculation as to whether a third member (the nematode) may be added to the physiologically specialized relationship which now exists between legume host and *Rhizobium* spp.

In so far as the cowpea–legume group is concerned, the nematode–nodule association is sufficiently widespread to encourage inquiry into its effects on: (*a*) the establishment and growth of the cowpea species used for green manuring throughout the Australian sugar cane belt; (*b*) the symbiotic nitrogen assimilation of such crops. These matters will continue to be investigated at the Macknade Experiment Station in North Queensland.

I thank Dr. J. B. Goodey, Rothamsted Experimental Station, for identifying the root-knot nematode.

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ENTOMOLOGY

Toxic Hazard from formulating the Insecticide Dimethoate in Methyl 'Cellosolve'

Dimethoate (O,O - dimethyl S - (N - methylcarbamoylmethyl) phosphorodithioate) is an effective systemic insecticide for use on plants[1,2], has shown promise as a chemotherapeutic agent for control of cattle grubs[4,5] and certain other insect pests of farm animals, and has high contact toxicity to house-flies and many other insects. The pure material, with a rat oral *LD*50 of about 600 mgm./kgm., is the least toxic to mammals of the systemic insecticides at present available for use in controlling plant pests. Commercial dimethoate is 2–4 times more toxic to rats than the pure compound, and repeated recrystallization or chromatography is required to achieve the reduced mammalian toxicity of the pure material. Several investigations have been reported on the chemical[6] and biological[7–9] degradation of dimethoate.

During the purification of commercial dimethoate, a fraction was separated which potentiated the rat oral toxicity of pure dimethoate. Addition of 2–10 per cent of this fraction to pure dimethoate potentiated its toxicity (rat oral *LD*50) by 3–4 times, a finding which at least partially explains the difference in toxicity between the pure and commercial material. This fraction also potentiated the toxicity of malathion and O,O-dimethyl S-carbamoylmethyl phosphorodithioate to the rat. The potentiator appears to be effective only with certain species, since the commercial material was more toxic than the pure compound to rats, guinea pigs, rabbits and

hens, but not to mice, pheasants, locusts, aphids and flies. With rats the potentiator was active by the oral and intra-peritoneal routes but not following dermal administration. On demethylation of dimethoate by reaction with salts of O,O-dimethyl phosphorodithioic acid, O,O,S-trimethyl phosphorodithioate and a potentiating material were formed. The potentiator, also formed by the reaction of dimethoate with lithium chloride, may be a salt of O-methyl S-(*N*-methylcarbamoylmethyl) phosphorothioic acid or a closely related compound. On analogy with the potentiation of pure dimethoate by O-ethyl O-*p*-nitrophenyl phenylphosphonothionate, tri-*o*-cresyl phosphate and tri-*o*-cresyl phosphorothionate[10], it would appear that the potentiating impurity in commercial dimethoate might act by reducing the efficiency of the dimethoate detoxification mechanism acting through hydrolysis of the carboxyamide grouping.

Methyl and ethyl 'Cellosolve' (2-methoxy- and 2-ethoxyethanol) have excellent solvent characteristics for the formulation of organophosphorus insecticides, particularly where a high degree of systemic activity is desired after application to foliage. As a result of routine toxicity checks on the properties of technical dimethoate formulated in methyl 'Cellosolve', an unexpected toxic hazard was observed. The rat oral *LD*50 decreased on storage from an initial 150–250 mgm./kgm. to 30–40 mgm./kgm. after seven months storage in England. After nine months storage under tropical conditions the *LD*50 was less than 15 mgm./kgm., and after storage at 100° C. for 63 hr. in the laboratory the *LD*50 was 8 mgm./kgm. The mammalian toxicity increased several-fold before any change in insecticidal activity was evident. Further development of this unstable formulation was immediately stopped.

Chromatography by described procedures[7,9] of the decomposed dimethoate in methyl 'Cellosolve' yielded fourteen phosphorus-containing products. The degradation involved hydrolysis at the amide and all the ester groupings, a marked loss of thiono sulphur, and replacement of both the O-methyl and *N*-methylamino groupings by 2-methoxyethanol. No evidence was obtained for the formation of pyrophosphates or thionopyrophosphates. The most toxic fraction was purified and identified as an O,O-dialkyl S-(*N*-methylcarbamoylmethyl) phosphorothiolate with probably one, but possibly both, methyl groups of dimethoate replaced by 2-methoxyethyl groupings. This compound was less toxic to flies than dimethoate, but had a rat oral *LD*50 of about 1 mgm./kgm. and a mouse intra-peritoneal *LD*50 of about 0·5 mgm./kgm. The increase in toxicity to mammals of the decomposed dimethoate formulation was greater than that attributable solely to this single toxic product. Since no other single component was toxic enough to account for the discrepancy, it appears that a potentiation of toxicity also occurred among the materials in the dimethoate - methyl 'Cellosolve' formulation.

The relationship of stability to toxicity of dimethoate formulated in a number of solvents was investigated. Little if any hydrolysis or change in mammalian toxicity occurred in non-hydroxylic solvents. Polyhydroxylic solvents resulted in stability during short storage without the formation of highly toxic degradation products. Of several monohydroxylic solvents, only methyl and ethyl 'Cellosolves' resulted in formulations highly toxic to mammals on short-term storage at 70° C. From this work a commercial formulation was developed which showed no significant change of toxicity after 162 days storage at 40° C.

The potential hazard which could have arisen is not unique for dimethoate, since O,O-dimethyl S-(*N*,*N*-dimethylcarbamoylmethyl) phosphorodithioate, O,O-dimethyl S-(1,2-dicarbethoxyethyl) phosphorodithioate (malathion), O-methyl O-(2,4,5-trichlorophenyl) phosphoramidothionate (Dow *ET*-15) and O,O-dimethyl O-(2,4,5-trichlorophenyl) phosphorothionate (Dow *ET*-57) were also found to show a several-fold increase in mammalian toxicity after reaction with methyl 'Cellosolve' at 70° C. for eight days.

When 'Cellosolves' are to be used in formulating phosphorothionate insecticides, the possible ester and amide exchange reactions to yield products of increased mammalian toxicity should be carefully investigated. A more complete account of these investigations will appear elsewhere.

Publication of this communication is approved by the Director of the Wisconsin Agricultural Experiment Station, and by the Directors of Fisons Pest Control, Ltd. The investigation was supported in part by a Haight Travel Fellowship from the Graduate School of the University of Wisconsin to one of us (J. E. C.), and by grants from the U.S. Public Health Service, National Institutes of Health, and from the U.S. Atomic Energy Commission (Contract No. *AT*(11–1)–64, project No. 14). We thank Dr. E. F. Edson, Dr. G. S. Hartley, Mr. A. J. Lambie and Mr. P. Carter of Fisons Pest Control, Ltd., and Mrs. Lydia McBride of the University of Wisconsin, for their encouragement and assistance.

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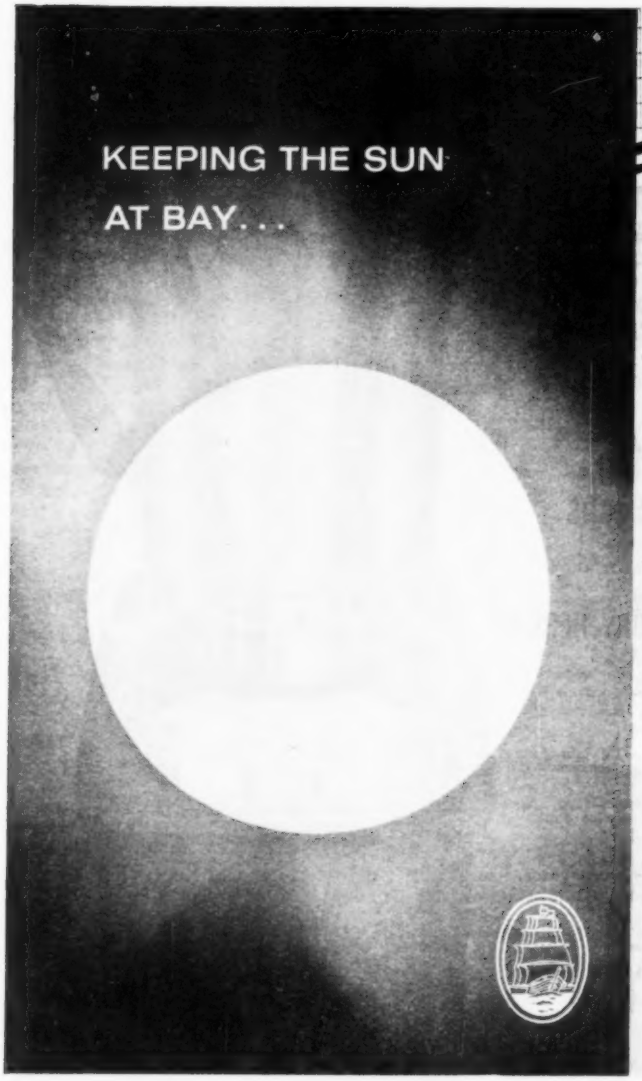
Lysine as a Mosquito Attractant

PREVIOUS work has indicated that attractive factors other than carbon dioxide are present in the vapour from mammalian blood[1] and body exudations[2]. A distillate obtained from mammalian blood proved highly attractive to *Culex pipiens*[3]. It has been recently reported that a mixture of nine biological acids and bases was attractive to *C. pipiens* and



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Anopheles maculipennis at concentrations down to 0·05 per cent, although none of the compounds was attractive when tested individually[4].

Our experiments on *Aedes aegypti* were guided by an old report[5] that peptone and certain amino-acids had shown attractiveness for *A. sollicitans*, and by the fact that protein hydrolysates are employed successfully as baits for fruit flies. Control and experimental solutions were exposed on filter-paper in warm Petri dishes[1] in a cage containing mosquitoes maintained only on sugar-water; the number of approaches to the experimental solution, as compared to that to the control, was expressed as the attractiveness ratio. Of 16 different protein hydrolysates commercially available and tested in 10 per cent solution, 11 proved to be attractive. Of these, 8 were more attractive than ox blood plasma; on distilling them to dryness at 7 mm. mercury pressure and 37° C., the distillates of five of them proved significantly attractive.

Individual amino-acids were then tested, dissolved in distilled water in the relative amounts in which they occur in 10 per cent lactalbumin hydrolysate. Of the 17 tested, the only amino-acids to be significantly attractive were (with their attractiveness ratios): L-arginine 1·24, L-alanine 1·32, and L-lysine 3·84. A mixture of all the amino-acids except lysine showed an attractiveness ratio of 1·14; addition of lysine raised the attractiveness ratio to 2·80. At the buffered *p*H of 7·4, lysine showed an attractiveness ratio of 3·13, and raised the attractiveness ratio of the amino-acid mixture from 1·28 to 6·13.

L-Lysine hydrochloride was not attractive in acid solution, but became highly attractive in alkali (attractiveness ratio 2·59 at *p*H 7·4); L-lysine free base was attractive also in acid solution (attractiveness ratio 5·62 at *p*H 4·4). The hydrochloride of the unnatural enantiomorph D-lysine showed an attractiveness of 1·20 at *p*H 6·5 and of 3·70 at *p*H 11·6. The potency of L-lysine at *p*H 10 was such that in 0·001 per cent and 0·0001 per cent (1 p.p.m.) solutions its attractiveness ratios were respectively 5·95 and 2·86. When a 0·7 per cent solution of L-lysine was distilled at 7 mm. mercury pressure and 37° C., the distillate showed an attractiveness ratio of 7·73 and gave a positive ninhydrin test.

When a mixture of 0·88 per cent L-lysine and 0·24 per cent L-alanine was chromatographed through a 50 × 1·2 cm. column of 'Dowex 50W-X4' resin[6] and the successive eluate fractions tested, the attractiveness of alanine appeared at 40–50 ml. and that of lysine at 75–88 ml. after the addition of the sample to the column. When deproteinized lactalbumin hydrolysate (10 and 0·1 per cent solutions assayed) was similarly fractionated, the greatest attraction was at 66–90 ml., with a minor peak at 53 ml. The fraction at 87 ml. was tested by paper chromatography and found to contain L-lysine. When deproteinized ox blood plasma was chromatographed, the main peak of attractiveness was around 90 ml., with a smaller peak at 30–50 ml.; the amino-acid present in the 93- and 88-ml. fractions was identified as L-lysine. When deproteinized human blood plasma was fractionated, the main peaks were at 40–50 ml. and around 80 ml.; the fractions at 44 and 81 ml. were found to contain L-alanine and L-lysine respectively. In all the fractionations, a minor peak was found at about 120 ml., possibly due to L-arginine.

The results thus indicate that the most attractive principle in the protein hydrolysate and blood plasmas tested was L-lysine. Of possible contaminants, ornithine and asparagine showed no attractiveness, whereas ammonia, putrescine and cadaverine were strongly repellent at high concentrations and never became attractive on progressive dilution. L-Lysine proved attractive not only to the Orlando strain of *Aedes aegypti*, but also to strains from Penang, Key West and Trinidad. It was also attractive to field-caught *Aedes stimulans*, and to *Culex pipiens* at evening. A solution of L-lysine exposed in the cage stimulates the resting mosquitoes to take flight, and they react to it as to a guinea pig or human hand. The concentration of L-lysine in human blood[7] and sweat[8] is about 27 gm. per ml. Since it may be distilled from aqueous solution and is attractive at 1 p.p.m., L-lysine could thus be the main attractive factor of mammalian blood and body emanations.

Full details of the work will be published elsewhere. We are indebted to the Defence Research Board of Canada for financial support of these investigations.

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A Method of dissolving the Protective Spittle Masses of Frog Hopper Nymphs

During the course of biochemical investigations into the nature and composition of the spittle masses produced by cercopid nymphs (*Philaenus spumarius* L. and *Neophilaenus* sp.) it was observed that these masses decomposed within a few minutes of being placed in a 2/3 *N* solution of sulphuric acid.

Since Cercopidae are of considerable economic importance, especially *Aeneolamia varia saccharina* in the cane sugar industry, and are protected from the action of insecticides by the spittle which they produce, it was realized that the above observation might be utilized in the measures taken for their control.

It was shown in the laboratory that the rate of solution of spittle masses (Fig. 1) was dependent on the normality but largely independent of the nature of the acid, hydrochloric and nitric being as effective as sulphuric acid. Since the rate of solution is not only dependent on the normality of the acid, but also on size of spittle mass and amount of agitation, the values given in Fig. 1 therefore relate only to spittle masses of the size produced by late fourth and early fifth instar nymphs, and subjected to gentle agitation. Field trials were then carried out using sulphuric acid at various concentrations. This acid was chosen because of its low vapour pressure. Dieldrin (0·06 per cent), added as Shell 'Dieldrex', was added to each solution to kill exposed nymphs and thus prevent the production of new spittle masses. The results are given in Table 1, which also shows the effect of weather on both the rate and total destruction of spittle masses.

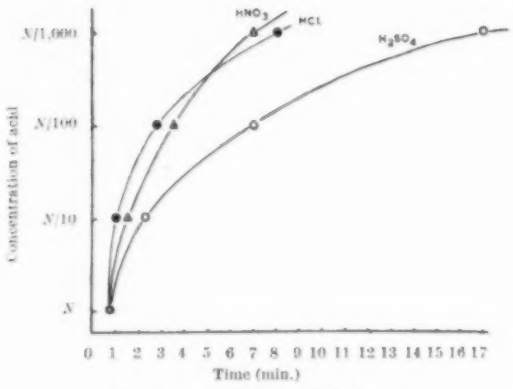

Fig 1. Rate of solution of spittle by acids

The phytotoxic effects of sulphuric acid on maize and oats, when sprayed as above at concentrations up to 2 *N*, were found to be negligible. Scorching of the leaves was produced by *N* and 2 *N* acid sprayed on at the rate of 100 gal./acre, but not by solutions of *N*/5 and *N*/10 acid. In neither case were subsequent growth and flowering affected by this treatment.

Similar results were found for grasses (species as in Table 1) although when using *N* acid the degree of scorching was distinctly greater. The use of *N* acid alone in this test resulted in a 95 per cent destruction of spittle masses within 48 hr.

Table 1. Percentage Destruction of Spittle Masses by Sulphuric Acid

Plots of grasses, each containing *Arrhenatherum elatius*, *Deschampsia caespitosa*, *Agrostis tenuis* and *Holcus lanatus*, were sprayed with solutions of sulphuric acid or water each containing 0·06 per cent dieldrin.

Test A. Carried out during a period of showery weather (total for the 3 days of the test: rainfall, 0·29 in.; sunshine, 15·5 hr.) on 4¼ sq. yd. plots sprayed at the rate of 110 gall./acre.

	Percentage destruction of spittle masses					
Time (days)	1		2		3	
N/5 + 0·06 per cent dieldrin	50	(41)	65	(59)	65	(62)
N/10 + 0·06 per cent dieldrin	38	(27)	59	(52)	62	(51)
Control (distilled water + 0·06 per cent dieldrin)	15		15		8	

Corrected percentage destruction in parenthesis.

Test B. Carried out during a period of dry sunny weather (total for the 3 days of the test: rainfall, 0·01 in.; sunshine, 17·6 hr.) on 5 sq. yd. plots sprayed at the rate of 100 gall./acre:

	Percentage destruction of spittle masses					
Time (days)	1		2		3	
N/5 + 0·06 per cent dieldrin	21	(28)	58	(62)	81	(81)
N/10 + 0·06 per cent dieldrin	38	(43)	51	(55)	85	(85)
N/50 + 0·06 per cent dieldrin	14	(21)	22	(28)	51	(51)
Distilled water + 0·06 per cent dieldrin	0	(8)	3	(11)	30	(30)
Control untreated	−9		−9		0	

Corrected percentage destruction in parenthesis.

These preliminary results therefore suggest that if sulphuric acid is added to solutions of acid-stable insecticides to give a final concentration of *N*/5, the nymphal mortality of Cercopids will be greatly increased. Using higher concentrations on crops not damaged by *N* and 2 *N* acid, an even greater mortality of nymphs can be achieved.

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BACTERIOLOGY

Microbial Production of Carbon Monoxide from Flavonoids

Aspergillus flavus degrades rutin to protocatechuic acid, phloroglucinol carboxylic acid, rutinose and carbon monoxide, the last-named being derived from carbon 3 of the flavonoid molecule[1,2]. The extent of distribution of this degradative pathway in micro-organisms and the structural requirements for the production of carbon monoxide were determined by comparing the amount of carbon monoxide produced after the growth of micro-organisms on various flavonoid compounds. The cultures studied were grown in sealed flasks of known volume[3]. A medium containing *N*—*Z* amine[1] was used when the substrates tested could be analysed by the aluminium chloride reaction. A synthetic medium[4] was employed with substrates that were difficult to determine directly and the amount of oxygen consumed was therefore used as the criterion of substrate utilization. Carbon monoxide and oxygen were determined by gas phase chromatography using a molecular sieve column.

The production of carbon monoxide from flavonoids is a common reaction in moulds but is absent in the bacteria tested (Table 1). As the recoveries of carbon monoxide are in general less than theoretical for the amount of substrate metabolized, there must be more than one pathway available to moulds for growth on flavonoid compounds.

A hydroxyl group in the 3-position is required for carbon 3 to be released as carbon monoxide (Table 2). Production of carbon monoxide is unaffected by the degree of saturation existing between carbons 2 and 3, or by the presence of a glycosidic bond in the 3-position (Tables 1 and 2).

Table 1. Production of Carbon Monoxide from Cultures Grown on Rutin, Quercitrin and Quercetin

Culture	Rutin		Quercitrin		Quercetin	
	Per cent theoretical CO‡	Per cent substrate used	Per cent theoretical CO‡	Per cent substrate used	Per cent theoretical CO‡	Per cent substrate used
Alternaria sp.	78	91	43	7	18	30
*Aspergillus flavus**	94	100	34	6	35	40
*Aspergillus niger**	87	96	70	46	17	51
Cephalosporium sp.	82	95	106	98	63	30
Diaporthe sp.	84	94	91	94	32	82
Fusarium sp.†	87	100	108	97	95	40
Penicillium sp.†	76	92	96	63	53	74
Pullularia sp.	82	99	88	25	16	44
Pseudomonas sp.*	0	98	0	62	0	40

* Representative of results for 3 strains.
† Representative of results for 2 strains.
‡ Calculated on the amount of substrate used.

Table 2. Effect of Substitution Pattern of Flavonoid Compounds on the Production of Carbon Monoxide by *Aspergillus flavus* PRL 1805

Substitution pattern	Δ-2,3 (flavone)	Δ-2,3; 3-OH (flavonol)	3-OH (flavanonol)	Nil (flavanone)
5,7,3',4'-(OH)$_4$	—	+ (quercetin)	+ (taxifolin)	—
5,7,4'-(OH)$_3$	0 (apigenin)	+ (kaempferol)	—	0 (naringenin)
7,3',4'-(OH)$_3$	—	+ (fisetin)	(fustin)	—
5,7,2',4'-(OH)$_4$	—	+ (morin)	—	—
5,7,3-(OH)$_3$-4'(OCH$_3$)	—	—	—	0 (hesperetin)

—, Not tested.
+, Carbon monoxide production.
0, Growth, but no carbon monoxide produced.

Table 3. Effect of substitution Pattern of Flavonoid Compounds on Growth of Two Fungi as indicated by Oxygen Utilization

Class	Compound	Substitution pattern	Percentage of oxygen used	
			PRL 1805	PRL 30*
Flavonol	Quercetin	3,5,7,3',4'-(OH)$_5$	25·4	43·6
,,	Morin	3,5,7,2',4'-(OH)$_5$	4·1	2·4
,,	Kaempferol	3,5,7,4'-(OH)$_4$	55·1	55·3
,,	Fisetin	3,7,3',4'-(OH)$_4$	10·5	6·3
,,	Robinetin	3,7,3',4',5'-(OH)$_5$	14·4	—
,,	Rhamnetin	3,5,3',4'-(OH)$_4$-7(OCH$_3$)	26·6	—
	Azaleatin	3,7,3',4'-(OH)$_4$-5-(OCH$_3$)	2·6	—
,,	—	3-(OH)-5,7,3',4'-(OCH$_3$)$_4$	2·6	—
,,	—	5-(OH)-3,7,3',4'-(OCH$_3$)$_4$	7·2	—
Flavanonol	Taxifolin	3,5,7,3',4'-(OH)$_5$-2,3-(H)$_2$	36	—
Flavone	Apigenin	5,7,4'-(OH)$_3$	38·3	39·8
Flavanone	Naringenin	5,7,4'-(OH)$_3$-2,3-(H)$_2$	63·1	—
Flavanol	Catechin	3,5,7,3',4'-penta-hydroxyflavan	12·6	6·9

* *Fusarium* sp.

A. flavus cannot readily utilize quercitrin (quercetin-3-rhamnoside), but does utilize the aglycone; quercetin was obtained from quercitrin by acid hydrolysis. This implies that the production of the glycosidase which splits the rhamnosidic bond is the factor limiting growth on this substrate. It would also appear that the production of this enzyme limits the growth of the *Alternaria* sp. studied on quercitrin.

The effect of a 3-hydroxyl group on the point of cleavage of flavonoid compounds has been noted by Booth *et al.*[5]. These authors found that mammalian systems degraded flavonoid compounds with a 3-hydroxyl group to yield a phenolic acid with a 2-carbon side-chain, while those without this group yielded a phenolic acid with a 3-carbon side-chain.

The position of the substituent groups (that is, hydroxyls and methoxy groups) does affect the utilization of flavonoid compounds by micro-organisms (Table 3). For example, these cultures did not readily utilize morin as a carbon source but did use quercetin and kaempferol. It can be shown by use of molecular models that this is a result of the steric hindrance of the 3-position by the presence of a 2'-hydroxyl group. This steric hindrance implies a change in the electron distribution pattern around carbons 2 and 3 and/or hydrogen bonding between the 2'- and the 3-hydroxyl groups. The 4-position is implicated as being an active centre in the enzymatic attack of flavonoids as catechin was not readily utilized as a carbon source. Similarly, the 5-position is implicated by the low utilization of fisetin, robinetin and azaleatin. As apigenin, naringenin and taxifolin were readily utilized as carbon sources, neither a double bond between carbons 2 and 3 nor a hydroxyl group in the 3-position is required for ready utilization of the flavonoid molecule. The presence of methoxy groups on the flavonoid molecule interferes with the utilization of these compounds as carbon sources by the micro-organisms studied. However, the presence of a single methoxy group in the 7-position is without effect.

Hattori and Noguchi[6] reported the isolation of the depside of phloroglucinol carboxylic acid and protocatechuic acid after the growth of *Pullularia fermentans* var. *candida* on rutin. As the pathway outlined by our work[1,2] results in a similar product, it is quite likely that the carbon monoxide-producing pathway was used by *P. fermentans* during growth on rutin.

Micro-organisms[7], plants[7] and animals[8] have been reported to produce carbon monoxide. This communication reveals that flavonoid compounds are a potential source for carbon monoxide production by moulds. These facts, together with reports that micro-organisms are known which oxidize carbon monoxide[9], suggest that carbon monoxide is an important, active, 1-carbon metabolite in the carbon cycle.

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Examination of *Leptospira pomona* by Gel Diffusion

In recent years, diffusible antigens of many bacteria and viruses have been demonstrated by the double-diffusion precipitation reaction in agar. Except for the work of Rothstein and Hiatt[1], who used the Oudin[2] technique in the study of chemically prepared fractions, we do not know of any investigation involving application of these methods in the study of *Leptospira*. This communication describes the results of an antigenic analysis of the four sub-serotypes of *Leptospira pomona*, attempted by diffusion of antigens and antibodies in agar.

Employing Mansi's[3] modification of Ouchterlony's[4] technique and hyperimmune sera prepared in rabbits, one common major line of precipitation was noted between antigen and antibody reservoirs when four antigenic sub-types were reciprocally examined against each other. However, differences in the line patterns were detected in the homologous systems; strains *pomona*, *C–B* and *C*-164 giving two reaction zones and strains *S*-91 and *G*-6 (Pande and Sekariah, 1960 [5]) producing only one line. These findings were confirmed with absorbed sera.

When fractions 1, 2 3 and 4 prepared from these sub-types, on the lines of Schneider[6], were tested against the homologous whole-cell antisera, a single line was detected with fractions 1 and 2 but no line with fractions 3 and 4, indicating that perhaps the latter antigens were located deep in the cell. Further tests showed that fractions 1, 3 and 4 were common to all sub-types within this serotype, while fraction 2 appeared to determine differences in serological reactivity.

When immune rabbit serum was examined against infected tissues, such as saline extracts of kidney lesions, a strong reaction was seen, whereas no reaction occurred between normal rabbit serum and infected tissues or suspensions and extracts of *Leptospira*. It has been found that 5 per cent formalin and 50 per cent glycerine do not destroy the antigen, and the test can be carried out satisfactorily on infected tissues preserved with these reagents.

It is intended to use this method in investigating field specimens obtained from suspected cases of leptospirosis in domesticated animals in India.

This test has also been successfully applied to detect antibodies in suspected sera when positive specimens were found to produce a single line of reaction within 2–3 hr. in the slide modification of the gel-diffusion test[7]. Precipitins could be detected by a comparable titre in the plate test. Further investigation is in progress to evaluate the diagnostic sensitivity and reliability of this method, on a comparative basis, the results of which will be reported in detail elsewhere.

We are indebted to Col. M. B. Starnes and Mr. A. D. Alexander, Division of Veterinary Medicine, Walter Reed Army Institute of Research, Washington 12, D.C., who kindly supplied the four sub-types of *L. pomona* and the homologous antisera.

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Localization of a Protease in the Cell of *Escherichia coli*

The cells of *Escherichia coli* contain a protease during their whole growth-cycle. This protease is inactive in living cells and its presence can be demonstrated only after disruption of the cell structure[1]. In connexion with the study of the function of this protease in the metabolism of intracellular proteins its localization in the cell was also investigated.

Spheroplasts were prepared from a 4-hr. culture of *E. coli B* by Lederberg's method[2] using penicillin. 20–30 per cent of the protease activity was transferred to the medium during the preparation of the spheroplasts. Because a part of the spheroplasts was disintegrated and their cellular proteins made soluble at the same time, it can be presumed that a greater part of the enzyme thus liberated is of intracellular origin. The spheroplasts were disrupted by osmotic shock in 0·01 *M tris* at *p*H 8·0 with 5×10^{-3} *M* magnesium chloride. The material was then centrifuged in the cold at 10,000*g* for 10 min. in an MSE centrifuge, the sediment washed with the buffer and again spun down. The combined supernatants were centrifuged for 1 hr. in a cooled Phywe ultracentrifuge at 105,000*g*, the pellet resuspended in the buffer and again spun down. The sediment at 105,000*g* exhibited a characteristic absorption at 257 mμ. The protease activity was determined with casein labelled with iodine-131 substrate[3] and referred to mgm. of protein, on one hand, and expressed as per cent of the whole amount of the enzyme, on the other. A loss of about 20 per cent of the enzymatic activity occurred during these operations.

It was found that the enzyme is present mainly in the cytoplasm and in the fraction which sediments at 10,000*g* and contains the cytoplasmic membrane and

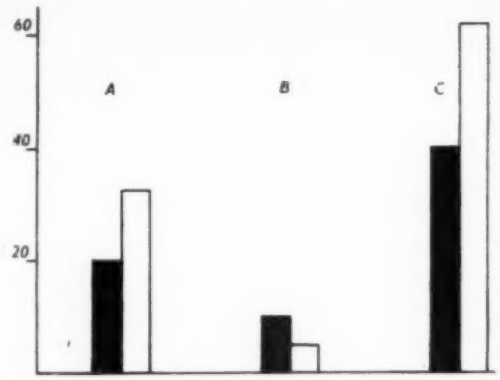

Fig. 1. Localization of a protease in cellular fractions of *E. coli*. *A*, Cytoplasmic membrane fraction; *B*, ribosome fraction; *C*, cytoplasm. Black columns, activity in μgm. of casein hydrolysed by 1 mgm. of protein during 1 hr. at 37° C.; white columns, percentage of total amount of protease

remains of the cell wall. Only a very small part of the whole amount of enzyme was present in the fraction of ribosomes which sedimented at 105,000*g* (Fig. 1). Enzymatic activity in the ribosome fraction probably is not due only to contamination, because the protease activity, related to mgm. of proteins, amounts in this fraction to about one-half of that of cytoplasmic membrane and cannot be completely removed by washing. A certain amount of active protease present in the ribosome fraction in the *E. coli* cell is analogous to the localization of the peptidase[5]. The ribosomes of *E. coli* also contain a ribonuclease[6] which is present in an inactive form and is activated after the disruption of ribosomes by ethylenediamine tetraacetic acid (EDTA) or urea. An attempt was made to verify the possibility that the inactive form of protease was present, and the influence of these substances on the activity of the protease in the fraction which sediments at 105,000*g* was therefore studied. The enzymatic activity was found to be reduced by EDTA at a concentration of 1×10^{-2} *M* by 70–80 per cent and the enzyme was completely inactivated by 4 *M* urea. The decrease in activity caused by EDTA was about the same in the fraction of ribosomes and in the cytoplasm and thus the presence of inactive protease in the ribosomes appears unlikely. The results obtained from fractions isolated from disrupted spheroplasts were checked by using material homogenized in the bacterial press[7]. It was found that in this case the enzyme was also distributed quite evenly between the fractions sedimenting at 10,000*g* and the cytoplasm. Here, too, only a small part of the whole amount of protease was found in the fraction of ribosomes.

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VIROLOGY

Presence in Horse Serum of Two Inhibitors of Avid A2 Influenza Virus Strains

RECENTLY it has been shown[1-3] that normal sera from some animals contain substances which inhibit specifically the avid[4] *A2* influenza virus strains. Attention has been paid to these substances, as they exhibit not only hæmagglutination-inhibiting activity, as the α-inhibitors, but also virus-neutralizing activity.

In our laboratory two inhibitors of avid *A2* influenza virus strains, showing different mobilities in the electric field and differing also in other properties, were isolated from normal horse serum.

The faster-moving inhibitor, designated as glycoprotein inhibitor, was isolated from the lyophilized sulphosalicylic acid filtrate of the serum[5] by extraction with an equal volume of 90 per cent phenol at 65° C. for 30 min.[6]. The water layer was freed of phenol by dialysis and then lyophilized. The substance obtained showed a single boundary on electrophoresis and sedimentation in the analytical centrifuge. It was of a glycoprotein nature, containing 18–20 per cent hexoses, 14·8–16 per cent sialic acid, 11·5–12·5 per cent hexosamines and 38–40 per cent polypeptides. 1 mgm. of this glycoprotein contained 6,400–12,000 hæmagglutination-inhibiting units against 4 hæmagglutination units of the avid *A2* (Singapore) 57 influenza virus strain (eighth egg passage) and neutralized 100–1,000 $TCID_{50}$ of this virus up to 1 : 1,024 dilution. The action of a 0·1 per cent solution of crystalline trypsin at *p*H 8·0 and 37° C. for three days lowered the inhibitory activity of the inhibitor 50–100 times. 400–800 units of receptor destroying enzyme have split 43–50 per cent of the total sialic acid from 2 mgm. of the glycoprotein, without affecting the activity of the inhibitor.

The slowly moving inhibitor, designated as γ-globulin inhibitor, was isolated from horse serum by precipitation with a 0·01 per cent solution of 'Neokal *B*' (commercial preparation of a butylnaphthalenesulphonate) in phosphate buffer *p*H 6·4 and 0·02 ionic strength. The serum was mixed at 0° C. with the 'Neokal' solution in the ratio 1 : 20, the precipitate separated by centrifugation, redissolved in saline and dialysed against distilled water. During the dialysis the euglobulins, containing the bulk of the biological activity, were precipitated. They were used in this work without further purification. The electrophoretic and sedimentation patterns of this substance showed the presence of two components. 1 mgm. of the γ-globulin inhibitor contained 400–800 hæmagglutination-inhibiting and 512–1,024 virus-neutralizing units.

Both inhibitors isolated from horse serum were specific, in that they reacted only with the avid *A2* influenza virus strains. Potassium periodate in 0·001–0·005 *M* concentrations completely inactivated the inhibitors at room temperature in 15 min.

The two inhibitors were separated from their mixture by paper electrophoresis using diethylbarbiturate buffer *p*H 8·6 as electrolyte and recovered by elution of 1-cm. strips. The maxima of the hæmagglutination-inhibiting activity coincided with those of proteins, this being in agreement with the results obtained by other authors[7] with unfractionated horse serum.

Table 1. HÆMAGGLUTINATION-INHIBITING ACTIVITY OF THE GLYCOPROTEIN AND γ-GLOBULIN INHIBITORS AFTER DIFFERENT TREATMENTS

Treatment, fraction, original concentration	Hæmagglutination-inhibiting units per mL.	
	Glycoprotein inhibitor	γ-Globulin inhibitor
'Neokal', supernatant, 2 mgm./ml.	32,768	0
'Neokal', precipitate, 35 mgm./ml.	no precipitate	16,384
Sulphosalicylic acid, filtrate, 20 mgm./ml.	131,072	0
Sulphosalicylic acid, precipitate, 35 mgm./ml.	no precipitate	2,048
Heating at 100° C. for 30 min., supernatant, 5 mgm./ml.	131,072	64
Heating at 100° C. for 30 min., precipitate, 5 mgm./ml.	no precipitate	0

Table 2. SOME PROPERTIES OF THE HORSE SERUM INHIBITORS AGAINST AVID *A2* INFLUENZA VIRUS STRAINS

Properties	Glycoprotein inhibitor	γ-Globulin inhibitor
Sedimentation constant (S_{20})	3·66 *S*	14·7 *S** and ~ 5·9 *S*
Mobility in the electric field at *p*H 8·6	with α-globulins	between β- and γ-globulins
Solubility in distilled water	soluble	insoluble
Hæmagglutination-inhibiting units per mgm.	13,107	409–1,638
Virus-neutralizing units per mgm.	1,024	512–1,024

* Main component.

The differences in some properties of the inhibitors (solubility, sedimentation-rate, mobility in the electric field, hæmagglutination-inhibiting and virus-neutralizing activities) as well as the changes in their hæmagglutination-inhibiting activity after heating at 100° C. and treatment with 'Neokal', sulpho-salicylic acid and phenol are presented in Tables 1 and 2.

On the basis of the results so far obtained we may conclude that normal horse serum contains at least two specific inhibitors of avid *A2* influenza virus strains. The inhibitor moving faster in the electric field is an acid serum glycoprotein, and the slow one—so far not characterized in detail—is of a γ-globulin nature.

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SOIL SCIENCE

Soluble Aluminium in Plants and Soils

HIGHLY soluble aluminium concentrations in extracts of certain acid soils were first noted at least as early as 1904[1]. It has been commonly explained as being due to aluminium ions held by chemical and physical means within the mineral part of the soil[2]. This mechanism usually requires a close

correlation between soil *p*H and the concentration of soluble aluminium[3]; but such correlation does not always occur.

The idea of accumulation of aluminium by plants is very old[4]. 'Aluminium accumulators', defined as plants which habitually accumulate appreciable quantities of aluminium in their tissues, have been regarded as a source of aluminium in the soil[3]. An exhaustive study of the aluminium content of leaves of plants in herbaria and from the British Colonies was made by Chernery[5,6]. Without considering the aluminium content of soils, he assumed that those specimens with more than 1,000 p.p.m. soluble aluminium according to the aluminon test would be accumulating species and those with less present in the leaves would be normal species. Various authors[7,8] have since used these data to explain soluble aluminium accumulation in soils, while Lovering[9] has suggested that it is a possible origin of bauxites and laterites.

Certain species are also thought to be dependent on a sufficiently high content of soluble aluminium in the soil for normal healthy growth[2]. Simonson[10] has suggested that there should therefore be indicator species to help in soil survey work. As Hutchinson[2] points out, there are undoubtedly many chemical forms in which soluble aluminium can occur in soils, and it can probably exist in appreciable quantities at all levels of *p*H.

During a detailed soil survey of an area of 30,000 acres on the coastal plain of British Guiana, a special study was made of the occurrence of species in the natural vegetation cover in relation to the distribution of soluble aluminium in the soil. The soluble aluminium could not have come in from outside, while drainage conditions and past history precluded the objections put forward by Chernery[11] in reply to Polynov[7]. Both high and low concentrations occurred at field *p*H values in the range < 4–$8{\cdot}5$. No correlation with plant species was obtained, but there was a marked direct relationship between the return and accumulation of organic matter in the soil and the amount of soluble aluminium present in the same layer. Where secondary bush was allowed to grow, higher figures were obtained for both the organic matter content and the soluble aluminium in adjoining areas which had had a similar land-use history up to 1936.

The outstanding thing about the climax flora and distribution of soluble aluminium content was the wide range of tolerance of all species (Table 1). In an adjoining area[12], concentrations of soluble aluminium up to 13,986 p.p.m. alumina have been reported in the surface A_1 horizon with a similar but rather stunted vegetation cover. Clearly these species grow equally well under conditions of both high- and low-soluble aluminium content in the soil. This might be expected since the flora has entered the area with high concentrations from the adjacent interior[12], where the soils have very low values for soluble aluminium.

The only explanation of these results would appear to be that the plants are absorbing aluminium from the soil, accumulating it and returning it with the soil organic matter. Owing to the action of earthworms (which live at *p*H values at least as low as 3·5), and other microfauna which mix up the organic matter with the upper mineral horizons at the drier sites, and the generally swampy conditions, there is an enrichment of the surface layers of the soil in organic matter and in soluble aluminium (probably as a chelate). In the absence of signs of any other processes, levels of soluble aluminium as high as 13,986 p.p.m. aluminium can only be obtained in this way.

Table 1. Tolerances of Soluble Aluminium Concentrations in the Root Zone of the Main Species in the Climax Floras of the Coastlands of British Guiana

Climax (ref. 16)	Species	Family	Soluble aluminium content of the root zone (Al^{3+} p.p.m.)
Palm marsh forest	*Adiantum intermedium*	Polypodiaceae	120–570
	Cecropia angulata	Urticaceae	6–713
	Desmoncus sp.	Palmae	41–645
	Euterpe edulis	Palmae	63–2,962
	Miconia racemosa	Melastomaceae	63–645
	Montrichardia arborescens	Araceae	16–2,962
	Pentaclethra macroloba	Leguminosae	63–962
Swamp forest	*Mauritia flexuosa*	Palmae	120–2,962
	Mikania micrantha var. *congesta*	Compositae	120–760
	Pterocarpus officinalis	Leguminosae	179–1,200
	Tabebuia insignis var. *monophylla*	Bignoniaceae	160–2,962
Herbaceous swamp	*Blechnum serrulatum*	Polypodiaceae	91–2,962
	Cyperus luzulae	Cyperaceae	37–1,200
	Eleocharis interstincta	Cyperaceae	14–2,926
	Jussiena nervosa	Oenotheraceae	312–2,926
	Leersia hexandra	Graminae	16–2,962

The process could operate faster if a 'compound interest' effect operated. The whole idea of using artificial fertilizers is based on a similar principle. Even in leached tropical soils, accumulations from plant tissues cause the surface layer generally to be richer in plant nutrients than the deeper horizons. It would therefore seem not unreasonable to expect that the accumulation of soluble aluminium in leaves of plants would increase as the available supply of soluble aluminium in the soil is increased. There is some evidence for this. Church[14] and Stoklasa[15] found widely different values for the aluminium content of *Aspidium filix-mas*. Chernery[6] also reported two greatly differing amounts in the tissues of *Eleocharis equisitina* from different environments. Further work is now being carried out to verify these relationships.

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FORTHCOMING EVENTS

(Meetings marked with an asterisk • are open to the public)

Monday, February 13

BRITISH SOCIETY FOR THE PHILOSOPHY OF SCIENCE (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. E. Gombrich: "Theory and Observation in the Work of Leonardo da Vinci".

ROYAL INSTITUTE OF CHEMISTRY (at the North-West Kent College of Technology, Miskin Road, Dartford, Kent), at 7.30 p.m.—Prof. E. D. Hughes, F.R.S.: "Reaction Mechanisms".

Tuesday, February 14

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

ROYAL SOCIETY OF MEDICINE, PSYCHIATRY SECTION (at 1 Wimpole Street, London, W.1), at 5.15 p.m.—Prof. Eugene Popov: "Soviet Psychiatry".

BRITISH INSTITUTION OF RADIO ENGINEERS, ELECTRO-ACOUSTICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. J. Jessop: "Some Psycho-acoustic and Engineering Aspects of Hearing Aid Design".

INSTITUTION OF THE RUBBER INDUSTRY, LONDON SECTION (at the National College of Rubber Technology, Holloway Road, London, N.7), at 5.30 p.m.—Dr. W. D. Rae: "Technical Aspects of Rubber to Metal Bonding". 7 p.m.—Research Topics by College Research Personnel.

UNIVERSITY OF LONDON (at Imperial College of Science and Technology, London, S.W.7), at 5.30 p.m.—Prof. J. S. Rowlinson: "The Impact of Chemical Physics on Technology" (Inaugural Lecture).

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. R. A. McCance: "The Control of Acid-base Stability in the Newly Born".• (Tenth of fifteen lectures on "The Scientific Basis of Medicine", organized by the British Postgraduate Medical Federation.)

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Technical Teacher Training" opened by Dr. F. T. Chapman.

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. W. D. Jarvis: "The Occurrence of Fire-side Corrosion in Modern Steam Generators".

ROYAL INSTITUTE OF CHEMISTRY (at Norwood Technical College, Knight's Hill, West Norwood, London, S.E.27), at 7 p.m.—Mr. T. McLachlan: "The Work of a Public Analyst".

Wednesday, February 15

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 p.m.—Discussion Meeting on "The Meteorological Implications of the Distribution of Radioactive Fall-out".

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Mr. Christopher Scott: "Research on Mail Surveys".

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Prof. P. M. S. Blackett, F.R.S.: "Science and Technology and the Developing Countries" (Hinchley Memorial Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. D. Rudd: "A General Theory of Depreciation of Engineering Plant".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. S. L. Rowles: "Biochemistry of Enamel".• (Last of three lectures on "The Scientific Basis of Dentistry" organized by the British Postgraduate Medical Federation.)

SOCIETY OF ENVIRONMENTAL ENGINEERS (at the Imperial College of Science and Technology, South Kensington, London, S.W.7), at 6 p.m.—Meeting on "The Development and Testing of Small Electronic Components".

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (joint meeting with the London Section of the Royal Institute of Chemistry, at University College, Gower Street, London, W.C.1), at 6.30 p.m.—Dr. J. S. Anderson, F.R.S.: "Some Recent Advances in Inorganic Chemistry".

SOCIETY FOR ANALYTICAL CHEMISTRY, BIOLOGICAL METHODS GROUP (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Mr. C. J. Threlfall: "The Use of Enzymes in Analysis".

Thursday, February 16

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. F. C. Webb: "Useful Micro-organisms".•

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. J. E. Amoore: "Arrest of Mitosis in Roots by Oxygen-lack or Cyanide" and "Dependence of Mitosis and Respiration in Roots Upon Oxygen Tension"; Mr. A. G. Morton: "The Induction of Sporulation in Mould Fungi".

INSTITUTION OF MINING AND METALLURGY (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers.

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. E. R. Reifenberg: "Solution of the Plateau Problem for m-dimensional Surfaces of Varying Topological Type".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. G. P. Lewis: "The Role of Bradykinin in the Control of Local Blood Flow".• (Eleventh of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

INSTITUTION OF ELECTRICAL ENGINEERS (at the Central Hall, Westminster, London, S.W.1), at 6 p.m.—Mr. L. J. Davies: "Transistors and All That" (Faraday Lecture).

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. G. E. Bessey: "An Investigation of the Properties of Mortars".

PLASTICS INSTITUTE (at the Royal Institution, Albemarle Street, London, W.1), at 6.30 p.m.—Prof. G. Gee, F.R.S.: Swinburne Award Address.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (at Manson House, 26 Portland Place, London, W.1), at 7.30 p.m.—Symposium on "Fungus Diseases". Contributors: Prof. W. St. C. Symmers, Dr. Ian Murray and Dr. Mary Marples.

BRITISH INSTITUTE OF RADIOLOGY (at 32 Welbeck Street, London, W.1), at 8 p.m.—Mr. B. B. Milstein, Mr. D. A. W. Edwards, and Mr. F. R. Berridge: "The Mechanism of the Cardia".

Friday, February 17

INSTITUTE OF NAVIGATION (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—Symposium on "The Admiralty Chart", introduced by the Hydrographer of the Navy.

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. W. B. Thompson: "A Comprehensive Introduction to Plasma Physics".

ROYAL SOCIETY OF MEDICINE, EPIDEMIOLOGY AND PREVENTIVE MEDICINE SECTION (at 1 Wimpole Street, London, W.1), at 5.30 p.m.—Discussion on "Study of Control Methods in Tuberculosis". Speakers: Dr. James Grant, Dr. E. L. Feinmann, and Dr. K. M. Martischnig.

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. T. A. Blanco White: "Patent Protection for Chemical Inventions".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—The Right Hon. The Lord Adrian of Cambridge, O.M., F.R.S.: "Dreaming".

Saturday, February 18

LONDON COUNTY COUNCIL (at the Horniman Museum, London Road, Forest Hill, London, S.E.23), at 3.30 p.m.—Mr. E. Roe: "Journey to Jebel Al Akhdar (Arabia)".•

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER (with a good honours degree in either botany or agricultural botany and a special interest in mycology or plant pathology) IN THE DEPARTMENT OF AGRICULTURAL BOTANY—The Registrar, University College of Wales, Aberystwyth (February 18).

SENIOR TECHNICIAN (with appropriate H.N.C. or C. and G. Final Certificate or equivalent) IN THE PHYSICS DEPARTMENT, for servicing electronics equipment—The Registrar, Brighton Technical College, Richmond Terrace, Brighton, 7 (February 18).

LECTURER IN ELECTRIC TRACTION IN THE DEPARTMENT OF ELECTRICAL ENGINEERING—Head of the Electrical Engineering Department, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7 (February 20).

LECTURER OR ASSISTANT LECTURER (with special qualifications in applied mathematics); and a LECTURER or ASSISTANT LECTURER (with special qualifications in pure mathematics) IN THE DEPARTMENT OF MATHEMATICS OF THE FACULTY OF SCIENCE—The Registrar, The University, Manchester 13 (February 20).

BIOCHEMIST (honours graduate, with some research experience) to assist Dr. R. M. C. Dawson on isotopic studies on lipid metabolism in rumen micro-organisms and in the ruminant digestive tract—The Secretary, Institute of Animal Physiology, A.R.C., Babraham, Cambridge (February 23).

SENIOR LECTURER (with an honours degree in mathematics, and preferably a higher degree and some experience of research) IN APPLIED MATHEMATICS at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 25).

ASSISTANT LECTURER (with a good honours degree and special interests in mineralogy) IN GEOLOGY—The Registrar, King's College (University of London), Strand, London, W.C.2 (February 28).

LECTURER/ASSISTANT LECTURER (preferably with experience in the field of gas discharge or solid state physics) IN THE DEPARTMENT OF PHYSICS—The Registrar, University College of North Staffordshire, Keele, Staffs. (February 28).

LECTURER (with a university degree in electrical engineering, subsequent experience in research, in teaching, or in industry, and a knowledge of the fundamentals of nuclear engineering) IN ELECTRICAL ENGINEERING at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (February 28).

Soil Survey Officer (male, with a first- or second-class honours degree in science) for the Soil Survey of Scotland—The Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (February 28).

Lecturer (with a special interest in geomorphology and/or economic geography) in Geography—The Secretary, The Queen's University, Belfast (March 1).

Senior Lecturer or Lecturer in Physics at the School of General Studies, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, March 4).

Assistant Lecturer in Physical Chemistry—The Registrar, The University, Hull (March 6).

Lecturer and an Assistant Lecturer (men or women graduates) in the Department of Zoology—The Secretary to Council, Westfield College (University of London), Hampstead, London, N.W.3 (March 6).

Lecturer (with an honours degree in engineering or science with research and/or professional experience in one of the fields of radio communications, radio physics, or information theory) in Electrical Engineering at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, March 6).

Lecturer or Assistant Lecturer (with a special interest in plant physiology or biophysics) in Botany—The Registrar, University College, Singleton Park, Swansea (March 11).

Technical Officer (with a university degree in science or equivalent qualification and interested in the application and development of techniques for teaching and research in botany and/or biochemistry) in the Department of Botany, to be responsible for the general supervision and maintenance of the laboratories and the control and training of technical staff—The Registrar, University College, Singleton Park, Swansea (March 11).

Lecturer in Psychology at the University of Auckland, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, March 15).

Post-doctoral Research Fellow in Organic Chemistry for work which will involve a chemical study of the biosynthesis of pteridines, under the direction of Dr. H. C. S. Wood—The Secretary, The Royal College of Science and Technology, George Street, Glasgow, C.1 (March 15).

Professor of Pure Mathematics at Rhodes University, Grahamstown, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, March 20).

Senior Lecturer in Physics in the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, March 31).

Senior Lecturer in Medical Statistics in the Department of Public Health and Social Medicine—The Secretary, The University, Edinburgh (April 1).

Agricultural Chemist (with a good honours degree in agricultural chemistry or chemistry, and at least two years postgraduate research experience in agricultural chemistry) in Kenya, to take charge of research projects into soil and plant nutrition problems of coffee—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD. 63/7/050/C1.

Assistant Systematic Botanist (honours graduate in botany or agricultural botany)—The Secretary, National Institute of Agricultural Botany, Huntingdon Road, Cambridge.

Editorial Assistant (with a university degree in science or technology, and preferably at least two years postgraduate experience in science or industry)—The Manager, *Nature* Office, Macmillan and Co., Ltd., St. Martin's Street, London, W.C.2.

Lecturer (preferably with a special interest in deformation and fracture, a knowledge of solid mechanics, and experience in some industrial field) in Metallurgy in the Department of Materials—The Recorder, College of Aeronautics, Cranfield, Bletchley, Bucks.

Lecturer (with geochemical qualifications and familiar with one or more of the following techniques: optical or X-ray spectrography, silicate or radioactive analysis) in Pure Geochemistry—Prof. D. Williams, Department of Geology, Imperial College of Science and Technology, London, S.W.7.

Master to teach Physics to AS level and some Mathematics to O level—The Headmaster, Westminster School, 17 Dean's Yard, London, S.W.1.

Master to teach Physics to AS level; Chemistry to O level; and, if possible, some junior Biology and Mathematics—The Headmaster, Bloxham School, Banbury, Oxon.

Research Assistant to help with current research on an immunological project connected with rheumatoid arthritis—The Pathologist, Stoke Mandeville Hospital, Aylesbury, Bucks.

Senior Lecturer (qualified to direct research) in Physics—Clerk to the Governing Body, Northern Polytechnic, Holloway, London, N.7.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Handlist of Darwin Papers at the University Library, Cambridge. Pp. 72. (Cambridge: At the University Press, 1960. Published for the University Library.) 10*s.* [1111

Supplement to the Catalogue of Lewis's Medical, Scientific and Technical Lending Library, including a Classified Index of Subjects, with the names of those authors who have treated upon them—Supplement 1957–1959. Pp. 306. (London: H. K. Lewis and Co., Ltd., 1960.) 10*s.* 6*d.* net. (To subscribers to the Library, 5*s.* net.) [1411

Research Defence Society. Conquest Pamphlet No. 12: Animal Experiments in the Diagnosis of Human Disease: Outstanding questions posed and answered by the Research Defence Society. Pp. 8. (London: Research Defence Society, 1960.) 6*d.* [1411

Science Museum, London. Book Exhibitions No. 4: Historic Books on Mining and Kindred Subjects. Pp. 32. (London: Science Museum, or H.M. Stationery Office, 1960.) 1*s.* 6*d.* [1411

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 122: Poultry Mites, Lice and Fleas. Pp. 8. (Belfast: Ministry of Agriculture, 1960.) [1411

Agricultural Research Council. A Bibliography of Farm Buildings Research, 1945–1958. Part 4: Buildings for Cattle. Pp. 84. (London: Agricultural Research Council, 1960.) 4*s.* 6*d.* [1411

Bulletin of the British Museum (Natural History). Zoology. Vol. 7, No. 1: Hearing in Cetaceans: Evolution of the Accessory Air Sacs and the Structure and Function of the Outer and Middle Ear in Recent Cetaceans. By F. C. Fraser and P. E. Purves. Pp. 1–140 + plates 1–53. 80*s.* Vol. 7, No. 2: Les Types d'Harpagophoridae de R.I. Pocock Conservés du British Museum (Natural History), (Myriapodes, Diplopodes). Par J. M. Demange. Pp. 141–179. 15*s.* (London: British Museum (Natural History), 1960.) [1411

Annual Report of the Medical Research Council of Ireland, 1959. Pp. 58. (Dublin: Medical Research Council of Ireland, 1960.) [1711

Other Countries

Indian Forest Bulletin No. 171 (5), (New Series). Entomology: A List of Insect Pests of Forest Plants in India and Adjacent Countries. (Arranged Alphabetically according to the Plant Genera and Species, for the use of Forest Officers.) Part 6: List of Insect Pests of Plant Genera 'O' to 'K'. By R. N. Mathur and Balwant Singh. Pp. 91. (Delhi: Manager of Publications, 1960.) Rs. 7.25 nP.: 11*s.* 6*d.* [1011

Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture, Bruxelles. Comptes Rendus de Recherches, No. 25 (Octobre, 1960): Travaux de Centre de Chimie Physique Agricole. Pp. 232. (Bruxelles: Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture, 1960.) 270 francs. [1011

Report of the King Institute of Preventive Medicine, Guindy, for the period from 1st April, 1956, to 31st March, 1957, by Dr. S. Govindarajan; and Report of the Government Analyst, Madras, for the period from 1st April, 1956, to 31st March, 1957, by Sri S. Narayana Ayyar. Pp. i + 108. Report of the King Institute of Preventive Medicine, Guindy, for the period from 1st April, 1957, to 31st March, 1958, by Dr. S. Govindarajan; and Report of the Government Analyst, Madras, for the period from 1st April, 1957, to 31st March, 1958, by Sri S. Narayana Ayyar. Pp. i + 121. (Guindy, Madras: King Institute of Preventive Medicine, 1960.) [1011

Canada: Department of Mines and Technical Surveys. Geological Survey of Canada. Bulletin No. 60: Canadian Fossil Arthropoda Eurypterida, Phyllocarida and Decapoda. By M. J. Copeland and Thomas E. Bolton. Pp. ix + 84 (11 plates). 1.25 dollars. Memoir No. 303: Surficial Geology of Sturgeon Lake Map-Area, Alberta. By E. P. Henderson. Pp. vii + 108 (13 plates). 1 dollar. (Ottawa: Queen's Printer, 1960.) [1111

Travaux de l'Institut Scientifique Chérifien, Rabat. Série Géologie et Géographie Physique, No. 8: Les Conglomérats du Bas Oued Bou-Regreg et la Flore du Carbonifère du Jebel Bakach, Région de Rabat (Maroc). Par Guy Cogney et Paule Danzé-Corsin. Pp. 54 + 8 planches. (Rabat: Institut Scientifique Chérifien, 1960.) [1111

Rubber Research Institute of Malaya. Annual Report, 1959. Pp. ii + 141. (Kuala Lumpur: Rubber Research Institute of Malaya, 1960.) [1411

United States Department of the Interior: Geological Survey. Bulletin 1116-B: Geophysical Abstracts, No. 181, April–June, 1960. By James W. Clarke, Dorothy B. Vitaliano, Virginia S. Neuschel, and others. Pp. iii + 129–279. 40 cents. Bulletin 1121-A: Classification of Wisconsin Glacial Deposits in Northeastern Ohio. By George W. White. Pp. iii + 12. 15 cents. Water-Supply Paper 1314: Compilation of Records of Surface Waters of the United States, through September, 1950. Part 10: The Great Basin. Prepared under the direction of J. V. B. Wells. Pp. v + 485 + 1 plate. Water-Supply Paper 1451: Quality of Surface Waters of the United States, 1956. Parts 5 and 6: Hudson Bay and Upper Mississippi River Basins, and Missouri River Basin. Prepared under the direction of S. K. Love. Pp. ix + 349. 1.25 dollars. Water-Supply Paper 1487: Geology and Ground-Water Resources of the Lower Little Bighorn River Valley, Big Horn County, Montana. By E. A. Moulder, M. F. King, D. A. Morris, and F. A. Swenson. Pp. viii + 223 + 13 plates. Water-Supply Paper 1495: Geology and Ground Water in Napa and Sonoma Valleys, Napa and Somona Counties, California. By Fred Kunkel and J. E. Upson. Pp. v + 252 + 5 plates. Water-Supply Paper 1536-A: Borehole Geophysical Methods for Analysing Specific Capacity of Multiaquifer Wells. By Gordon D. Bennett and Eugene P. Patten, Jr. Pp. iii + 25. (Washington, D.C.: Government Printing Office, 1960.) [1711

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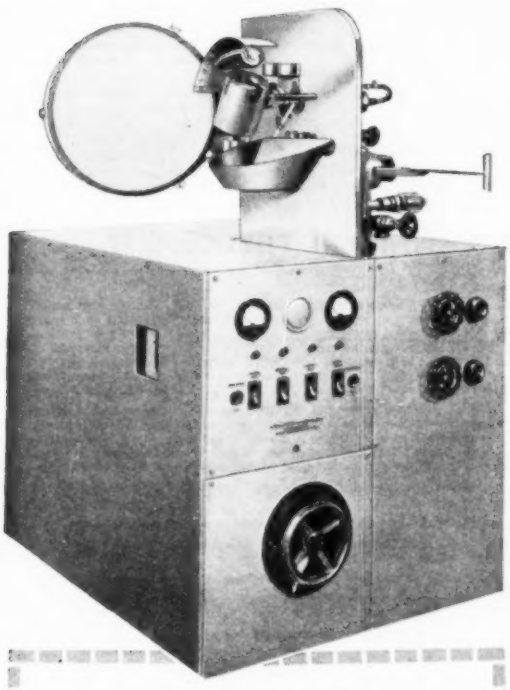

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APPOINTMENTS VACANT

GOVERNMENT OF WESTERN NIGERIA

vacancy for

FISH FARMER

Applications are invited from suitably qualified candidates for the post of Fish Farmer in the Fisheries Division of the Ministry of Agriculture and Natural Resources.

Qualifications: Applicant should be able to interpret results of fish cultural experiments; must have long and up-to-date practical experience in fish breeding with its ancillary problems, in the building of simple earthen dams, the transportation of live fish, and in the stocking, feeding, maintenance of ponds; and must have knowledge of fish diseases and their cure.

Duties: To plan and execute fish cultural experiments to determine the fastest growing of indigenous species, other than the Tilapia species, most suited to the needs of the Western Region, or to investigate the possibility of introducing exotic fast-growing species that will not upset the natural balance of the rivers of the Region. To initiate and supervise the actual building and maintenance of simple, earthen dams for community fish ponds, ponds for private individuals, educational institutions and local councils. To breed selected species for ultimate transplantation into existing fish ponds and reservoirs of the Region, and to work out simple and cheap containers for the transportation of live fish within the Region both for stocking and marketing.

Conditions of appointment: On contract for one or two tours each of 12 to 18 months. Salary is between £1,722 to £2,160 per annum according to experience since qualifying. In addition, gratuity is paid at the rate of £37 10s. for each completed three months service. Free first-class passages for officer and his family on first appointment and when proceeding on leave; free medical treatment for officer and his family. Accommodation is provided at low rentals.

Method of application: Application should be completed in triplicate on the prescribed form obtainable from the Official Secretary (Recruitment Branch), Office of the Agent-General for Western Nigeria, 178/202 Great Portland Street, London, W.1, from whom further particulars may also be obtained. Closing date March 4, 1961

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

POST-DOCTORAL FELLOWSHIP IN PLANT ECOLOGY

(No.: 146/139)

The Organization's **Division of Tropical Pastures, Cunningham Laboratory, Brisbane, Queensland,** invites applications for a Post-doctoral Fellowship for three years in Plant Ecology from applicants with experience in autoecology, both laboratory and field studies. The Cunningham Laboratory maintains a research farm and several field stations providing extensive facilities for research with plants and soils and for growing plants under controlled environment conditions and provides headquarters for a research team of 35 graduates from five C.S.I.R.O. Divisions working on the development of improved pastures in North-Eastern Australia.

The appointee is required to initiate studies on the autoecology of *Heteropogon contortus* L. Beauv. (black spear grass). This perennial native species occurring over some 40 million acres of rangeland north of Brisbane limits forage value and assumes dominance in many areas and information is needed on the variation present within the species and its requirements for growth and reproduction.

Salary: Dependent on qualifications and experience, not less than £A.1,620 per annum, up to a maximum of £A.2,265 per annum.

AGRONOMIST/PLANT PHYSIOLOGIST

(No.: 500/132)

The Organization's **Irrigation Research Station, Griffith, N.S.W.,** invites applications for the position of Agronomist/Plant Physiologist from Honours graduates in Science or Agricultural Science (or equivalent qualifications) with advanced training and research experience in plant physiology or plant nutrition, preferably with some research on fruit crops. The Research Station, situated 300 miles north of Melbourne and 400 miles west of Sydney, has 103 acres of irrigated land in a 14 in. rainfall area where the main products are citrus, stone fruit, pome fruit, vines, rice, fat lambs and wool.

The appointee will be required to carry out research on the nutrition and development of citrus as a dominant fruit tree in inland irrigation areas. Long-term manurial and management trials on oranges have been in progress for some time. Laboratory facilities available where plants can be grown in closely controlled environmental conditions which are also equipped for radio-active isotope work on growing plants.

Salary: Dependent on qualifications and experience, within the ranges £A.1,510 to £A.2,265 per annum.

Salary for a woman will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further details of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting relevant Appointment No.) should be addressed by March 25, 1961.

UNIVERSITY COLLEGE OF WALES
ABERYSTWYTH

Applications are invited for the post of Assistant Lecturer in the Department of Agricultural Botany to take up duties on October 1, 1961. Applicants should possess a good honours degree in either Botany or Agricultural Botany and should have a special interest in Mycology or Plant Pathology. Salary scale: £800 by £50 to £900, under 26 years of age on appointment, £850 by £50 to £950, over 26 years of age on appointment, plus superannuation benefits and children's allowances.

Further particulars can be obtained from the Registrar, to whom applications should be sent, together with the names of two persons to whom reference may be made, not later than February 18, 1961.

INSTITUTE OF CANCER RESEARCH, Royal Cancer Hospital. Research Assistant required in Royal Marsden Hospital, Fulham Road, S.W.3, for radioactive isotope work, particularly development of tracer techniques and whole-body counting. Applicants should hold O.N.C. in Applied Physics, G.C.E. (A) in Physics, or similar qualifications. Appointment on M.R.C. scale £410 to £860.—Apply with details of qualifications, experience, and names of two referees to the Secretary, 33 Sumner Place, S.W.7, quoting ref. 301/B/50.

GOVERNMENT OF NORTHERN IRELAND
SENIOR SCIENTIFIC OFFICER

Applications invited for pensionable post in Agricultural Entomology Research Division, Ministry of Agriculture. Qualifications: Honours degree in science or agriculture plus at least two years postgraduate study and research in plant nematology. Preference will be given to those having a sound knowledge of the systematics of eelworms and with practical experience in laboratory techniques and the applied aspects of plant nematology under United Kingdom conditions. Salary scale: £1,342 to £1,654. A candidate with special qualifications, training or experience may enter above minimum. Successful candidate may be required to undertake teaching duties in Faculty of Agriculture in Queen's University, Belfast. Preference for ex-Servicemen.

Application forms obtainable from Secretary, Civil Service Commission, Stormont, Belfast, 4, must be returned with copies of two recent testimonials, by February 22, 1961.

TECHNICIAN (FEMALE) REQUIRED FOR new, expanding Physics Laboratory. Work will be concerned chiefly with diagnosis and treatment using radioactive isotopes. Commencing salary up to £495 per annum depending on age and qualifications/experience. — Further particulars from Hospital Secretary, Dudley Road Hospital, Birmingham, 18.

UNIVERSITY OF DUBLIN
TRINITY COLLEGE
RESEARCH STUDENT IN PHARMACOLOGY

Applications are invited for a Research Studentship in Pharmacology, for work on naturally occurring neuromuscular blocking agents. It is expected that the successful candidate will have had experience in one of the following fields: medicine, chemistry, biochemistry, pharmacology. The student will be required to register for the degree of M.Sc. or Ph.D. of the University of Dublin. The salary will be not less than £400 per annum.

Applications (four copies), giving full particulars of career and experience, and the names and addresses of three referees, should reach the Registrar, Trinity College, Dublin, not later than February 27, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for the post of Lecturer in Physical and/or Inorganic Chemistry in St. Salvator's College, St. Andrews. Salary scale £1,050 to £1,850, with an efficiency bar at £1,400; starting salary according to qualifications and experience. F.S.S.U.; family allowance; grant towards expenses of furniture removal.

Six copies of applications, with the names of three referees, to be lodged by March 11, 1961, with the Joint Clerk to the University Court, College Gate, St. Andrews, from whom further particulars may be obtained.

MIDDLESEX COUNTY COUNCIL EDUCATION COMMITTEE

BRUNEL COLLEGE OF TECHNOLOGY
Principal: Dr. J. Topping, M.Sc., D.I.C.
DEPARTMENT OF CHEMISTRY
RESEARCH FELLOWSHIP IN LIPID CHEMISTRY

Applications are invited for the Unilever RESEARCH FELLOWSHIP IN LIPID CHEMISTRY, tenable for one year in the first instance, but renewable annually up to a maximum period of three years.

Salary is £1,500 per annum, subject to deductions for superannuation and National Insurance contributions.

Candidates should preferably hold a university degree or Diploma in Technology in chemistry or biochemistry and have had research or appropriate industrial experience in the field of lipid chemistry. The successful candidate should have some experience of modern techniques and will be required to undertake co-operative study with the Central Middlesex Hospital Research Group working in the lipid field. The successful candidate should be able to commence on April 1, 1961, or as soon after as possible.

RESEARCH ASSISTANT IN LIPID CHEMISTRY

Applications are also invited for a RESEARCH ASSISTANTSHIP IN LIPID CHEMISTRY which has been established as part of a D.S.I.R. Award.

The salary of the Research Assistantship, tenable for one year in the first instance and renewable annually up to a maximum period of three years, will be £870 rising to £905, subject to deductions for superannuation and National Insurance contributions.

Candidates should hold a good degree in chemistry or biochemistry and preferably have some research or industrial experience in the field of lipid chemistry. Duties to commence as soon as possible.

Further particulars and forms of application may be obtained from the Registrar, Brunel College of Technology, Woodlands Avenue, Acton, W.3, to whom they should be returned within fourteen days of the appearance of this advertisement.

C. E. GURR, M.Sc., Ph.D.,
Chief Education Officer.

UNIVERSITY COLLEGE OF SWANSEA

Applications are invited from suitably qualified candidates for the following posts: Pure Mathematics, A Research Fellowship in the Theory of Probability and/or Mathematical Statistics. Physics, two Assistant Lectureships or Lectureships (one post will be Superintendent of Laboratories). Chemistry, an Assistant Lectureship or a Lectureship. Geology, an Assistant Lectureship or a Lectureship, with particular interest in Mesozoic stratigraphy and palaeontology. A Research Demonstratorship. Geography, two Assistant Lectureships. Zoology, an Assistant Lectureship and a Lectureship.

Salary Scales: Lectureships, £1,050 by £50 to £1,400 by £75 to £1,850 per annum. Assistant Lectureships, £800 by £50 to £950 per annum. Research Demonstratorships, £650 to £700 per annum. Research Fellowships, within the range £800 to £1,100 per annum. F.S.S.U. benefits and family allowances.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies) must be received not later than Saturday, March 11, 1961.

UNIVERSITY OF LONDON KING'S COLLEGE

Applications are invited from those of British nationality for a Research Assistant in the Wheatstone Laboratory for research on cathodoluminescence, scintillation properties, etc., of certain elementary crystals. The appointment will normally be made for at least three years. The salary will depend upon qualifications and experience but will be initially in the range £800 to £1,000 per annum, together with membership of the F.S.S.U.

Applications (three copies), with a list of degrees, publications, etc., and the names of two referees, should be sent not later than March 5, 1961, to Professor F. C. Champion, Department of Physics, King's College, Strand, W.C.2.

CHEMICAL RESEARCH ASSISTANT/Technician, preferably with experience of steroid chemistry, to work with team investigating aspects of chemical endocrinology in relation to human biology and genetics.—Apply, giving two referees, Dr. J. M. Tanner, Institute of Child Health, Great Ormond Street, W.C.1. Closing date February 23.

UNIVERSITY OF LONDON

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

Applications are invited for the post of Lecturer in the Department of Bacteriology and Immunology. Duties include assistance in teaching and class preparation. The Lecturer will be expected to engage in research under supervision or to assist in research. Previous research and teaching experience are not essential, but candidates must possess a good medical qualification and have had some laboratory experience. The salary scale will be £1,350 by £100 to £2,150 by £50 to £2,250.

Forms of application and further particulars may be obtained from the Dean, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1.

WELLCOME RESEARCH LABORATORIES

A vacancy exists in the Histology Laboratory for a graduate, preferably with veterinary qualifications, for work involving chronic toxicity and the testing of vaccines. No previous specialized experience is necessary.

Information regarding the post may be obtained from the Head, the Histology Laboratory, Wellcome Research Laboratories, Langley Court, Beckenham, Kent, to whom applications, giving qualifications and experience, should be addressed.

RHODES UNIVERSITY

PORT ELIZABETH, SOUTH AFRICA

Applications are invited for the vacant post of Lecturer in Geography from July, 1961. The salary scale is £1,170 by £60 to £1,650 per annum. A vacation savings bonus, as in the Public Service, is also payable. Previous experience and academic qualifications may be taken into account in fixing the commencing salary.

Full particulars and application forms may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in South Africa and London, on March 20, 1961.

UNIVERSITY OF MELBOURNE

SENIOR LECTURESHIP IN PHYSICS

Applications are invited for the above-mentioned post. The salary range is £A.2,480 to £A.2,950 per annum and the commencing salary will be fixed according to qualifications and experience. Superannuation is provided by a scheme similar to the F.S.S.U. in Great Britain.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on April 28, 1961.

UNIVERSITY OF EXETER

Applications are invited for the post of Assistant Lecturer or Lecturer in Botany. Candidates should have a special interest in physiology. Salary scales: Lecturer, £1,050 to £1,850 (efficiency bar at £1,475); Assistant Lecturer, £800 by £50 to £950.

Further particulars may be obtained from the Secretary of the University. Closing date for applications (eight copies please) February 25, 1961.

UNIVERSITY OF LIVERPOOL

Applications are invited for three Leverhulme Postgraduate Fellowships, two in the Faculty of Science and one in the Faculty of Engineering, tenable for one year at the value of £600, and renewable for a second year.

Applications, three copies, stating age, details of qualifications and experience, publications, research work in progress and completed, and an outline of the proposed field of research, together with the names of two referees, should be received not later than March 1, 1961, by the Registrar, from whom further particulars may be obtained. Ref.: CV/N.

RESEARCH ASSISTANT WANTED AT Stoke Mandeville Hospital to help with current research on an immunological project connected with Rheumatoid Arthritis. The person appointed would work directly with the Pathologist undertaking the research. Salary £750 to £1,000 per annum according to qualifications.—Inquiries and applications, giving details of experience and the names of two referees, to the Pathologist, Stoke Mandeville Hospital, Aylesbury, Bucks.

U.S.A.

POST-DOCTORATE FELLOWSHIP AVAILable after May 15, 1961, but not later than August 15, 1961, for fundamental work in adsorption and catalysis. Salary $6,500 per annum, one month vacation. May continue for second or third year. Applicant should be qualified in vacuum techniques, and should have versatility in other physical-chemical techniques. Write Dr. S. Ross, Professor of Colloid Science, Rensselaer Polytechnic Institute, Troy, N.Y. (U.S.A.) to arrange interview with representative in London during March. Interview desirable but not necessary.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for the post of Lecturer/Assistant Lecturer in the Department of Physics. Salary in the scale £1,050 by £50 to £1,400 by £75 to £1,850 per annum (Lecturer), £800 by £50 to £950 per annum (Assistant Lecturer). Some preference may be given to applicants who have experience in the field of gas discharge or solid state physics.

Applications should reach the Registrar, The College, Keele, Staffs, from whom further particulars and application forms may be obtained, not later than February 28, 1961.

STOKE MANDEVILLE HOSPITAL

AYLESBURY

Assistant Biochemist required in the Area Pathology Laboratory based at the above Hospital. Applicants should possess first- or second-class honours degree in chemistry or biochemistry, or A.R.I.C. Whitley Council conditions of service. Salary £925 to £1,150 per annum after (for new entrants only) a probationary period. The post offers a wide variety of experience in a well-equipped and pleasant laboratory.

Applications, giving full details of qualifications, etc., together with names of two referees, to be forwarded to the Administrative Officer as soon as possible.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

RESEARCH STUDENTSHIPS IN GEOCHEMICAL PROSPECTING

Applications are invited from Geology Graduates for Research Studentships in applied Geochemistry (£600 to £800 per annum for two years) starting October 1, 1961. Successful applicants will carry out field work overseas during not more than two terms.

Apply Dr. Webb, Geology Department, Imperial College, London, S.W.7, before June 1.

UNIVERSITY OF SOUTHAMPTON

I.C.I. RESEARCH FELLOWSHIPS

Applications are invited for I.C.I. Research Fellowships in Biochemistry, Chemistry, Chemical Oceanography, Engineering and Physics. The appointments will date from October 1, 1961, or earlier if the selected candidate is available before that date. The salary, according to qualifications and experience, will be within the range £800 to £1,100 per annum. F.S.S.U. and children's allowance.

Applications (15 copies), containing list of publications and names of two referees, should be sent before March 11 to the Secretary and Registrar, The University of Southampton, from whom further particulars may be obtained.

PHARMACOLOGIST REQUIRED TO WORK in London for the first two years in an academic department and thereafter in a newly created Research Laboratory in London. Non-contributory Pension and Life Assurance Scheme and excellent salary; scope for promotion.—Write, giving full details of age, qualifications, experience and salary required to the Managing Director, Biorex Laboratories Ltd., 47/51 Exmouth Market, London, E.C.1.

OXFORD UNIVERSITY COMPUTING Laboratory invite applications for the Ferranti Fellowship in Computing, for one or two years from October 1, 1961. The successful candidate, who should have at least two years' research experience, will be expected to do original work in any field connected with computation or other application of digital computers, and will have access to a Ferranti Mercury. The Fellowship is open to candidates of any nationality, has a stipend of £900 per annum, and is subject to the provision of F.S.S.U., where applicable.—Applications, with details of academic and research experience, and the names of two referees, should be sent before July 31, 1961, to the Director, University Computing Laboratory, 9 South Parks Road, Oxford.

RESEARCH LABORATORY

AEI

A THEORETICAL PHYSICIST

is required to work on interesting problems concerning the interpretation of the results of experiments using the MERLIN reactor and its associated sub-critical facility. Suggestions for experimental work with these reactors would be encouraged. Digital and Analogue computers are available to assist the work, and the publication of results is also encouraged.

A good honours degree in physics or mathematics is essential. Some knowledge of reactor physics would be an advantage.

The Laboratory is situated in pleasant rural surroundings near Reading with fast train service to London.

5-day week
Pension Scheme

Apply in writing, quoting Reference No. R/TP/1, to the Administration Officer,

Research Laboratory
ASSOCIATED ELECTRICAL INDUSTRIES LIMITED,
Aldermaston Court,
Aldermaston, Berkshire

UNIVERSITY OF HONG KONG

SENIOR LECTURESHIP AND ASSISTANT LECTURESHIP IN BOTANY

Applications are invited for the above-mentioned posts. Preference will be given to applicants with experience in mycology and/or plant pathology (Senior Lectureship) and cytology and genetics (Assistant Lectureship) but persons experienced in other branches of botany should also apply. Annual salary (superannuable) is Senior Lecturer, £2,000 by £75 to £2,300 (man) or £1,500 by £60 to £1,740 (woman); Assistant Lecturer £1,375 by £50 to £1,525 (man) or £1,040 by £40 to £1,160 (woman). There is also an expatriation allowance of £250 a year for the Senior Lecturer and £225 a year for the Assistant Lecturer if applicable. The equivalent of income tax in the Colony is comparatively low. First-class sea passages are provided for expatriate staff and their families on first appointment and leaves. Accommodation at reasonable rental is provided for those receiving expatriation allowance.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Hong Kong and London, on March 11, 1961.

AUSTRALIAN NATIONAL UNIVERSITY

SCHOOL OF GENERAL STUDIES
SENIOR LECTURER OR LECTURER IN STATISTICS

Applications are invited for appointment to the above-mentioned post. Preference will be given to an applicant who is interested both in statistical theory and in the applications of statistics in economics. The salary range for a Senior Lecturer is £A.2,400 by £A.100 to £A.2,900 and for a Lecturer £A.1,640 by £A.90 to £A.2,360. Commencing salary will be in accordance with qualifications and experience.

Further information and the summary forms which must accompany an application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on March 25, 1961.

UNIVERSITY OF BRITISH COLUMBIA

PHYSICS

Applications are invited for appointments to the teaching and research staff as well as for post-graduate fellowships and scholarships for the Session commencing in September, 1961. There are specific vacancies at the Assistant Professor level in Optical Spectroscopy, Meteorology and Low Energy Theoretical Nuclear Physics. Applications in other fields of physics will also be considered.

Further information and a copy of an illustrated brochure describing the activities and facilities of the Department may be obtained by writing to G. M. Shrum, Head, Department of Physics, University of British Columbia, Vancouver 8, B.C. Professor Shrum expects to be in London from March 16 to 25 and will be pleased to arrange personal interviews. Inquiries should be directed to B.C. House, 1 Lower Regent Street, London, S.W.1.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

EXPERIMENTAL OFFICERS FOR PLASMA JET RESEARCH

Applications are invited from graduates in physics or chemistry interested in research in the field of high temperature gas dynamics. A plasma jet wind tunnel, capable of generating gas streams at stagnation temperatures up to 10,000° K., is under construction.

Two Experimental Officers are required: commencing salary £850 per annum in scale £850 by £30 to £940 by £40 to £1,100. The appointments are for two years in the first instance and are superannuable.

Applications to Head of Aeronautics Department, Imperial College, London, S.W.7.

UNIVERSITY OF LIVERPOOL

ACCELERATOR PHYSICIST

A post of Assistant Lecturer or Lecturer is available in the Department of Physics for an accelerator physicist. The holder will take part in the further development for research of the Department's 400 MeV. synchro-cyclotron, and will also undertake normal teaching duties. Applicants must be honours graduates in physics or electrical engineering, and they should have practical experience in applied physics, electronics, or electrical engineering. The initial salary will be in the range £900 to £1,650 per annum, with F.S.S.U. benefits.

Applications, stating age, qualifications and experience, together with the names of three referees, should be received not later than March 1, by the Registrar, from whom further particulars of the conditions of employment may be obtained. Ref.: CV/N.

THE BRITISH CERAMIC RESEARCH Association has vacancies for Chemists or Physicists to work in the Pottery Section of the Association. There is also a vacancy for an Organic Chemist to work primarily on adhesives and grouting materials. Good laboratory facilities are available. The post is permanent and progressive and carries superannuation provision under the Federated Superannuation System for Universities. Salary will depend on age, qualifications and experience, but will be in the range of £720 to £1,090 for a Scientific Officer, and £1,100 to £1,600 for a Senior Scientific Officer.—Applications, giving details of age, qualifications and experience, should be sent to the Director, The British Ceramic Research Association, Queens Road, Penkhull, Stoke-on-Trent.

UNIVERSITY OF LONDON: APPLICATIONS are invited for Imperial Chemical Industries Research Fellowships in Biochemistry, Chemistry, Chemotherapy, Engineering, Metallurgy, Pharmacology or Physics. The Fellowships will normally be tenable from October 1, 1961, for three years. Candidates should preferably have a Ph.D. degree or equivalent research experience. Stipends will be within the range of £900 to £1,100 per annum, with annual increments of £50 up to £1,100, the starting point within the range being dependent upon experience and qualifications. Family allowance and F.S.S.U.—Detailed regulations and application forms may be obtained from the Academic Registrar, University of London, Senate House, W.C.1. Applications must be received not later than April 15, 1961.

CHEMIST FOR FINE CHEMICALS/ PHARMACEUTICALS ANALYSIS

A qualified chemist is required to investigate and develop new analytical test methods in the field of synthetic drugs. The position, which is in the Research Organization of the Smith and Nephew Group, involves close collaboration with the team of Organic and Pharmaceutical Chemists engaged in the development of chemotherapeutic products. The Laboratories, which are located in a country district 25 miles north of London, are well equipped with modern instrumental methods of analysis.

Applicants should be under 35 years and have an honours degree in chemistry, or at least Graduate Membership of the Royal Institute of Chemistry. Salary will be according to age, qualifications and experience.

There is a Contributory Pension Scheme and working conditions are in accordance with modern practice. Write, giving full details of experience, age and salary required, to:

Research Manager (Administration), Smith & Nephew Research Limited, Hunsdon Laboratories, Ware, Herts.

NORTHERN POLYTECHNIC

HOLLOWAY, LONDON, N.7

Applications are invited from honours graduates or from students in their Final Year for appointment as Research Assistants in Chemistry to work under the direction of Dr. W. Gerrard on one of the following projects: inorganic and semi-inorganic polymers, organic chemistry of boron or phosphorus, base-function of organic compounds containing oxygen, organo-metallic chemistry. The work may involve gas chromatography, infra-red spectroscopy and nuclear magnetic resonance. Registration for the Ph.D. degree (London, Internal) will be effected. Chemists with industrial experience and interested in teaching would find this an excellent opportunity to test their suitability. Rate of pay, approximately £600 per annum.

Further particulars are obtainable from Dr. W. Gerrard, Head of the Department of Chemistry.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

Assistant Experimental Officer required in Physics Department to assist in studies of physical properties of dairy products—butter and cheese, etc. He will also be required to construct and modify experimental testing equipment in the department workshop, and skill in using a lathe would be advantageous. Candidates should possess H.N.C. or pass degree, or, if under 22, G.C.E. "A" level or equivalent. Starting salary within range £450 10s. (at 18) to £776 (at 26) in scale to £983; pension scheme.

Apply, naming two referees, to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/4.

BRADFORD INSTITUTE OF TECHNOLOGY

Applications are invited for the post of Chief Technician in the Departments of Biological Sciences and Pharmacy. Applicants should possess a Higher National Certificate, a Final City and Guilds Laboratory Technicians' Certificate or an equivalent qualification and have experience of technical work. Salary scale: £815 to £960 per annum.

Further particulars and forms of application may be obtained from the Registrar, Bradford Institute of Technology, Bradford, 7.

HENRY PATTEN,
Clerk to the Governors.

RESEARCH WORKER, BIOCHEMIST OR chemical pharmacologist, preferably with Ph.D. or equivalent experience, required to investigate the biochemical actions of drugs currently used in the treatment of mental illness. Spectrophotofluorimetric methods of analysis will be employed. The work will be carried out in conjunction with clinical studies on therapeutic action. Three-year appointment, commencing salary £850 to £1,100 depending on qualifications and experience.—Applications, with names of two referees, to Director of Clinical Research, Crichton Royal, Dumfries, from whom further details may be obtained.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

CHEMICAL ENGINEERS, PHYSICAL CHEMISTS OR PHYSICISTS

The Organization's **Chemical Engineering Section, Chemical Research Laboratories, Melbourne,** invites applications from Honours graduates for the two under-mentioned positions as Research Officer or Senior Research Officer. At least two years post-graduate research experience is normally required for appointment as Research Officer but enquiries are also invited from more recent graduates.

APPOINTMENT No. 608/14

The appointee will join a team applying modern techniques, including frequency response to the study of the dynamic characteristics and controllability of closed-circuit grinding and other solid-handling processes. Experience in some or all fields of servo mechanism and control theory, statistics and particle size analysis would be of value.

APPOINTMENT No. 608/15

To participate in fundamental research in the field of fluid dynamics and interphase mass transfer. In this work a new approach is being made to the problem of transport between two fluid phases and either a chemical engineer, or a physical chemist with an interest in reaction kinetics and/or surface chemistry would be suitable.

Salary : Dependent on qualifications and experience within the ranges £A.1,510 to £A.2,265 per annum, or £A.2,395 to £A.2,720 per annum.

By arrangement these appointments may be for an indefinite period or for a fixed term of three or five years.

CHEMIST OR BIOCHEMIST

(*No.* 130/468)

The Organization's **Division of Plant Industry, Canberra, A.C.T.,** invites applications from graduates majoring in Chemistry or Biochemistry for a position as Experimental Officer to participate in research on isolation, structure and properties of the chloro-phyll-protein complexes from plants.

The work, directed towards an understanding of the role of such complexes in photosynthesis, will involve a number of specialized chemical and physicochemical techniques, including electrophoresis, ultracentrifugation, light scattering and spectro fluorimetry. Experience in these techniques desirable but not essential.

Salary : Dependent on qualifications and experience within the ranges £A.1,070 to £A.1,620 per annum, or £A.1,620 to £A.1,950 per annum.

Salary for women will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid and for fixed-term contracts return fares also paid. Further particulars on conditions, etc., supplied on application to :

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London W.C.2.

to whom applications (quoting relevant Appointment number) should be addressed by March 11, 1961.

ENGLISH ELECTRIC VALVE CO. LTD.

Chelmsford, Essex

A Physicist or Mathematician is required for research on electron optical systems.

Applicants should possess a first- or second-class honours degree in physics or mathematics, and be preferably within age range 22 to 30.

Salary will take into account age and any previous relevant experience.

Apply to Department G.P.S., English Electric House, Strand, London, W.C.2, quoting reference N1595P.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

(Faculty of Technology in the University of Manchester)

Applications are invited for a Lectureship and two Assistant Lectureships in Physical, Organic or Inorganic Chemistry in the College, with corresponding title and status in the University of Manchester. The Department of Chemistry includes a large postgraduate school. Salaries in the scales £1,050 to £1,850 per annum (Lecturers) and £800 to £950 per annum (Assistant Lecturers) with F.S.S.U. and family allowances.

Conditions of appointment and form of application may be obtained from the Registrar, the Manchester College of Science and Technology, Manchester, 1. The last day for the receipt of applications is Saturday, March 4, 1961.

GOVERNMENT OF WESTERN NIGERIA

vacancies for posts of

VETERINARY OFFICERS

Applications are invited for several posts of Veterinary Officers.

Qualifications : Candidates must possess the Diploma or Membership of the Royal College of Veterinary Surgeons or a recognized equivalent qualification registrable in Nigeria. Some practical experience, preferably in cattle practice, after graduation would be an advantage.

Duties : As for field Veterinary Officer, with emphasis on the control of animal epizootics. Animal husbandry, nutrition, and the economic development of the resources of the animal industry are also included in the scope of duties.

Conditions of appointment : On contract for one or two tours of 12 to 18 months each in the first instance. Salary is between £1,554 to £2,316 per annum, according to experience since qualifying. In addition, gratuity is paid at the rate of £37 10s. for each completed three months service. Free first-class passages for officer and his family on first appointment and when proceeding on leave; free medical treatment for officer and his family. Accommodation is provided at low rentals.

Method of application : Application should be completed in triplicate on the prescribed form obtainable from the Official Secretary (Recruitment Branch), Office of the Agent-General for Western Nigeria, 178/202 Great Portland Street, London, W.1, from whom further particulars may also be obtained. Closing date March 4, 1961.

UNITED OXFORD HOSPITALS

Applications are invited for the post of Senior Technician in charge of the Cardiac Department of the Radcliffe Infirmary, Oxford. The Department is responsible for all forms of routine investigation connected with the advanced diagnosis of cardiovascular disease. In addition, it is closely associated with a University Department and is engaged in research requiring the design of prototype equipment. Applicants from I.M.L.T., Physics or Cardiological Grades, or those with similar scientific experience. Salary scale: £710 to £905 per annum.

Apply, naming two referees, to the House Governor, Radcliffe Infirmary, Oxford.

UNIVERSITY OF DURHAM

KING'S COLLEGE
NEWCASTLE UPON TYNE, 1

The Council of King's College invite applications for a Lectureship in Pure Mathematics. The commencing salary will be determined at a suitable point on the Lecturers' Scale (£1,050 to £1,850) according to the age, qualifications and experience of the successful applicant. F.S.S.U. and child allowance.

Further particulars may be obtained from the Registrar and Secretary of King's College, to whom applications, together with the names and addresses of three persons to whom reference may be made, should be addressed so as to reach him not later than March 4, 1961.

UNITED KINGDOM ATOMIC ENERGY AUTHORITY

RESEARCH GROUP

RESEARCH FELLOWSHIPS

valued between £850 to £1,700 per annum

tenable for one to three years for research in

Physics	Chemical Engineering
Chemistry	Electronics
Metallurgy	Biochemistry
Biology	Engineering

at

ATOMIC ENERGY RESEARCH ESTABLISHMENT, HARWELL, BERKS

ATOMIC ENERGY ESTABLISHMENT, WINFRITH, DORSET

RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS

and in Plasma Physics at present at Harwell, but later at

CULHAM LABORATORY, CULHAM, OXON

Closing date March 31 for election in May, 1961.

Full information may be obtained from the Secretary, Research Group Fellowship Board, c/o A.E.R.E., Harwell, Berks.

McGILL UNIVERSITY

DEPARTMENT OF CHEMISTRY

Post-doctoral appointments are available for studies in:

(1) Chemistry of the Upper Atmosphere (atom reactions, chemiluminescence, mass spectrometry).

(2) Nuclear and Radiochemistry.

(3) Studies in physico-chemical aspects of Immunochemistry.

(4) Physical Chemistry of Interfaces.

(5) Organic Chemistry of Wood and Cellulose.

Salary: $5,300 per year.

Applicants should submit official documents attesting to academic qualifications and at least two supporting letters to the Chairman, Department of Chemistry, McGill University, Montreal, Quebec, Canada.

GOVERNMENT OF WESTERN NIGERIA

vacancy for post of

GAME WARDEN

Applications are invited for the post of Game Warden.

Qualifications: Candidates should possess a University degree or diploma in Natural or Applied Science and have a knowledge of and interest in African fauna.

Duties include the organization of effective protection in existing Game Reserves, review of Reserve boundaries, and measures for wild animal preservation, and study and report on all aspects of wild life in the Region.

Conditions of appointment: On contract for one or two tours of 12 to 18 months each in the first instance. Salary is between £1,920 and £2,160 per annum according to qualifications and experience. In addition, gratuity is paid at the rate of £37 10s. per each completed three months service. Free first-class passages for officer and his family on first appointment and when proceeding on leave; free medical treatment for officer and his family. Accommodation is provided at low rentals.

Method of application: Application should be completed in triplicate on the prescribed form obtainable from the Official Secretary (Recruitment Branch), Office of the Agent-General for Western Nigeria, 178/202 Great Portland Street, London, W.1, from whom further particulars may also be obtained. Closing date March 4, 1961.

UNIVERSITY OF MANCHESTER

Applications are invited for the following posts in the Department of Mathematics of the Faculty of Science: 1. Lecturer or Assistant Lecturer with special qualifications in Applied Mathematics. 2. Lecturer or Assistant Lecturer, with special qualifications in Pure Mathematics. Duties to commence on October 1, 1961, or earlier in the case of the post in Applied Mathematics, and on October 1, 1961, in the case of that in Pure Mathematics. Salary scales per annum: Lecturer, £1,050 to £1,850, initial salary according to qualifications and experience; Assistant Lecturer, £800 to £950. Membership of F.S.S.U. and Children's Allowance Scheme.

Applications should be sent, not later than February 20, 1961, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

UNIVERSITY OF SHEFFIELD

Applications are invited for a post of Assistant Lecturer or Lecturer in Physics to begin duties as soon as possible. Salary scales: Assistant Lecturer, £800 by £50 to £950; Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850, with F.S.S.U. provision and family allowance. Initial salary on either scale according to qualifications and experience. A grant towards removal expenses will be made.

Further particulars may be obtained from the Registrar to whom applications (four copies), should be sent by February 25, 1961.

NORTHERN POLYTECHNIC

HOLLOWAY, LONDON, N.7

The Governing Body invites applications for appointment as Senior Lecturer in Physics to commence in September, 1961, or before. The work of the Department includes courses for the B.Sc. Special Degree (Internal of London University) and for the Dip.Tech. in Physics, and postgraduate studies. Applicants should be qualified to direct research. Burnham scale salary: at present £1,550 by £50 to £1,750 plus London allowance.

Apply for further particulars and form of application.

R. H. CURRELL, F.C.A.,
Clerk.

SARAWAK AND NORTH BORNEO

GEOLOGIST

Qualifications: First- or good second-class honours degree in geology. Field, research or commercial experience an advantage. Duties: Chiefly field mapping, main objects being the search for mineral wealth and testing known mineral deposits. Age: up to 40. Conditions: On contract for three years, with gratuity of 12½ per cent of salary. Salary, according to experience, in the scale £1,344 to £2,324 per annum. Free family passages. Education allowances. Quarters provided if available. Generous leave.

Apply to Director of Recruitment, Colonial Office, London, S.W.1, stating full name, qualifications and experience and quoting BCD.105/127/01/C1.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Applications are invited for appointment as Lecturer in Electric Traction in the Department of Electrical Engineering, to work with a Reader to establish new section for postgraduate teaching and research in this subject. Salary in range £1,050 by £50 to £1,400 by £75 to £1,850, plus £60 London allowance, family allowances, and F.S.S.U. membership. Appointment will be in upper range for candidate with appropriate qualifications. Thorough knowledge of machines and rectifiers is of more importance than extensive experience in traction.

Applications to Head of Electrical Engineering Department, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7, by February 20, 1961.

A LADY OVER 25, IS REQUIRED TO RUN the Company's library, which forms part of the Technical Information Department and covers a wide range of electronic and engineering subjects. She will be responsible for accessioning classification by U.F.C. and cataloguing and should have reached A.L.A. standard in these subjects. Typing is an asset.—Please send details of education and experience to the Personnel Manager, the Plessey Company Limited, Vicarage Lane, Ilford, Essex.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

PHYSICS DEPARTMENT

Applications are invited for the following posts in the photo-electronics section: Lecturer. Salary in range £1,050 by £50 to £1,400 by £75 to £1,550 (bar) by £75 to £1,850 per annum, plus £60 London allowance, family allowance, and F.S.S.U. membership. Duties include teaching General Physics and special Advanced Course, research in application of photo-electronics to nuclear physics, astronomy, space research, etc. Research Assistant (Academic) to assist research in application of photo-electronics to nuclear physics, astronomy, space research, etc. A good degree essential and some research experience preferable. Salary in range £700 to £1,100 per annum, depending upon qualifications. Family allowance and F.S.S.U. membership.

Apply, with full personal and academic details and names of two referees, to Professor J. D. McGee, Physics Department, Imperial College of Science and Technology, London, S.W.7.

THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY, GLASGOW

DEPARTMENT OF CHEMISTRY

Applications are invited for a Post-doctoral Research Fellowship in Organic Chemistry. The work, which is supported by the British Empire Cancer Campaign, will involve a chemical study of the biosynthesis of pteridines, under the direction of Dr. H. C. S. Wood. The appointment will date from October 1, 1961. The value of the Fellowship will be £850 to £1,000 per annum and will be tenable for one to two years.

Applications, giving full academic qualifications, details of research experience, and the names of two referees, should reach the Secretary of the College, George Street, C.1, by March 15, 1961.

DURHAM COLLEGES IN THE UNIVERSITY OF DURHAM

Applications are invited for the post of Lecturer in Applied Physics from October 1, 1961. Candidates should preferably have shown a special interest in microwaves and microwave devices, both vacuum and solid state. Candidates with a special interest in electronic circuits and switching devices may however be considered.

Applications (three copies), together with the names of three referees, should be sent not later than March 4, 1961, to the Secretary, 38 North Bailey, Durham, from whom further particulars may be obtained.

OLDCHURCH HOSPITAL ROMFORD, ESSEX

(709 Beds)

RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

MINERAL DRESSING

A young graduate aged 24 to 28 required by a Mining and Manufacturing Company to carry out Research and Development, in the north of England, in the beneficiation of their mineral products.

Salary will depend on qualifications and experience. Non-contributory Pension Scheme.

Write, giving full details of education, experience, etc., to Box No. 950, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

COUNTY LABORATORIES LIMITED

Manufacturers of Brylcreem, Macleans Tooth Paste, Silvikrin and many other famous toiletry and cosmetic products require the following graduates for their Product Research Laboratory.

Research Chemist, for formulation and development of toiletry and cosmetic products.

Research Biologist or Chemist, for work on Biochemistry and Physiology of teeth.

For both appointments relevant experience would be useful, but recent graduates would be accepted.

Working conditions are excellent, and the Company operates a Profit Participation and non-contributory Pension Scheme.

Apply to the

Personnel Manager,
County Laboratories Limited,
Beecham House West, Great West Road, Brentford, Middlesex.

Attractive careers in the

CANADIAN METEOROLOGICAL SERVICE

for young University graduates

The CANADIAN GOVERNMENT is seeking honours graduates, including 1959 graduates, in Physics and Mathematics, Engineering Physics or equivalent courses for appointment to its meteorological service.

The starting salary is $4,920 a year and there are numerous opportunities for advancement.

Those selected may be enrolled at the University of Toronto in the post-graduate course leading to the Degree of Master of Arts in Physics (Meteorology). On completion of this course they will be given further training on the job and then assigned to regular duties. Full salary is paid while training.

For details, write to

CIVIL SERVICE COMMISSION, OTTAWA, CANADA.
Please quote Competition No. 61-174.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3

A Scientific Assistant is required for the maintenance of physical instruments including spectrophotometers and radiochemistry equipment. Duties will also include certain routine measurements and demonstrations. The person appointed will be directly responsible to the Heads of the Departments of Chemistry and Pharmacy. Salary scale: £940 by £40 to £1,000 per annum.

Further details of the appointment available on application. Closing date for applications: February 18, 1961.

RESEARCH INSTITUTE (ANIMAL VIRUS Diseases), Pirbright, Surrey, invites applications for Assistant Experimental Officer or Assistant (Scientific) in Biophysics Department. Work involves application of physical-chemical methods (electron-microscopy, electrophoresis, ultracentrifugation, etc.) to study of viruses, mainly of foot-and-mouth disease. Applicants should have, or be studying for, H.N.C. Salary dependent on age and qualifications in Assistant Experimental Officer scale £625 at age 22 rising to £983, or Assistant (Scientific) scale £453 at age 22 rising to £723.

Applications to the Secretary.

NATURE

Applications are invited for a post on the editorial staff of NATURE.

A university degree in science or technology is essential, and preference will be given to a candidate who has worked in science or industry for at least two years since graduation.

Particulars and references should be sent to: The Manager, *Nature* Office, Macmillan and Co. Ltd., St. Martin's Street, London, W.C.2.

INSTITUTE OF CANCER RESEARCH, Royal Cancer Hospital. Research Assistant required for Chester Beatty Research Institute, Fulham Road, S.W.3, to work in field of radiation biology. Candidates with G.C.E. "A" level in biology and mathematics preferred. Salary according to age, experience and qualifications on M.R.C. Technical Officers' scales.—Apply, with names of two referees, to the Secretary, 33 Sumner Place, S.W.7, quoting ref. 301/B/51.

CIBA (A.R.L.) LIMITED

have a vacancy for

A CHEMIST

FOR WORK ON ADHESIVES

Candidates should be aged under 30 and must have an Honours Degree in Chemistry. They should also have at least three years experience in a position where fundamental knowledge has been applied to practical applications. This experience need not necessarily have been in the adhesives field, but preference will be given to candidates with experience of synthetic resins.

The work will consist of the formulation of synthetic resin adhesives to solve a variety of bonding problems.

Working conditions are excellent, staff benefits and salaries comparing very favourably with other companies. The factory is located in a pleasant country village eight miles outside Cambridge.

Applicants should write to the Assistant Secretary, CIBA (A.R.L.) Limited, Duxford, Cambridge, setting out full details and stating their present salary.

Medicinal Chemistry

Pfizer Ltd. wishes to make several new appointments in its Chemical Research Department. Chemists (with degrees or A.R.I.C.) and Technicians (with H.N.C.) are required for the small scale synthesis of new compounds of interest in the medicinal and allied fields. In order to maintain our present high standards, preference will be given to Chemists with a genuine interest in structure-activity relationships and with good practical experience.

The Company's terms of employment and working conditions are of high quality. Staff have a choice of residence in East Kent coastal and inland areas.

Please send details of yourself to the

PERSONNEL OFFICER (RESEARCH), PFIZER LTD., SANDWICH, KENT

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AGRICULTURAL & VETERINARY PRODUCTS

BRITISH INDUSTRIAL BIOLOGICAL RESEARCH ASSOCIATION, LTD.

APPOINTMENT OF DIRECTOR

Applications are invited for the post of Director of the British Industrial Biological Research Association, which has recently been formed with the support of the Department of Scientific and Industrial Research to undertake biological investigations into the properties of substances for use in, or in connection with, the production, processing and packaging of food and cosmetics. The Association is contemplating the immediate establishment of a research station at Leatherhead, Surrey, in proximity to other research establishments, and the first task of the Director will be to make proposals to the Council of the Association for the building of the laboratories, the recruitment of staff, the formulation of a research and testing programme, and the provision of administrative services.

Preference will be given to candidates of proved scientific and research attainment. A medical qualification is desirable, and candidates must have had wide general experience in the biological sciences with specialist experience in pharmacology, toxicology, or pathology. The starting salary will be about £4,000 per annum, depending on age, qualifications and experience, and appropriate pension arrangements will be made.

Applications should be sent by March 11 at the latest to the President of the Association, Professor A. C. Frazer, M.D., D.Sc., F.R.C.P., University of Birmingham Medical School, Birmingham 15.

SURREY EDUCATION COMMITTEE

EWELL COUNTY TECHNICAL COLLEGE REIGATE ROAD, EWELL

Required September 1, 1961, Assistant Grade "B" to teach Physics to G.C.E. "A" level and O.N.C. Applied Physics. Teaching, industrial or other experience an advantage. Salary, Burnham Technical Scale, Grade "B," £700 to £1,150, plus London allowance.

S.A.E. to Principal for particulars and application form.

GOVERNMENT OF WESTERN NIGERIA

vacancy for

AGRICULTURAL OFFICER

FIELD EXPERIMENTATION

Applications are invited for the post of Agricultural Officer, Field Experimentation.

Qualifications: A University degree in agriculture. Two years of suitable, organized postgraduate training, preferably with emphasis on the technique of field experimentation, is essential.

Duties involve the selection and testing of strains of grasses and legumes and their comparison with each other and with imported strains singly in mixtures; investigations of methods of establishment and maintenance of pastures and leys, including grazing routines; relieving other officers as required and general advisory duties, including training of Junior Technical Staff.

Conditions of appointment: On contract for one or two tours of 12 to 18 months each in the first instance. Salary is between £1,200 and £2,160 per annum according to qualifications and experience. In addition gratuity is paid at the rate of £37 10s. for each completed three months service. Free first-class passages for officer and his family on first appointment and when proceeding on leave; free medical treatment for officer and his family. Accommodation is provided at low rentals.

Method of application: Application should be completed in triplicate on the prescribed form obtainable from the Official Secretary (Recruitment Branch), Office of the Agent-General for Western Nigeria, 178/202 Great Portland Street, London, W.1, from whom further particulars may also be obtained. Closing date March 6, 1961.

McGILL UNIVERSITY

POSTGRADUATE ASSISTANTSHIPS IN CHEMISTRY

Applications are invited from persons qualified to pursue M.Sc. and Ph.D. work in Chemistry for Teaching and Research Assistantships. Stipends are dependent on the number of hours per week given to teaching work. The maximum is 12 hours per week, for which a Teaching Fellow will receive $1,800 to $2,000 for the months of October to May inclusive. Stipends may be supplemented by a summer grant of $800 for the months of June to September inclusive, provided that the applicant carries on work leading to the degree during this period.

Research opportunities are available in Analytical Chemistry, Inorganic Chemistry, Radiochemistry, Physical Chemistry, Colloid Chemistry, Immunochemistry, Organic Chemistry, and the Chemistry of Cellulose and Lignin.

For further information please write to:

The Chairman,
Department of Chemistry,
McGill University,
Montreal, Quebec, Canada.

UNIVERSITY OF NEW ENGLAND
ARMIDALE, NEW SOUTH WALES
LECTURER/SENIOR LECTURER IN AGRONOMY

Applications are invited for the above-mentioned position in the Faculty of Rural Science. The successful applicant will be a graduate with an appropriate degree and with postgraduate research and/or field experience in agronomy. The appointee will be required to give lectures in general agronomy, fodder conservation and cropping, supervise projects by advanced students, and to conduct research for which excellent facilities are available in Plant Physiology, Soil Science and Agronomy. Commencing salary will be fixed according to qualifications and experience within the range of £A.1,730 by £A.105 to £A.2,435 for a Lecturer, and £A.2,550 by £A.95 to £A.3,000 for a Senior Lecturer, plus a cost of living allowance at present amounting to £A.29 per annum. Provision is made for superannuation, travel and removal expenses, and assistance in buying or building a house. A residential college fellowship may be awarded to a single person.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on March 10, 1961.

UNIVERSITY OF LIVERPOOL

Applications are invited for the following posts in the Department of Physics. (a) Leverhulme Fellow and Lecturer. The initial salary will be within the range £1,050 to £1,650 per annum, depending upon age and experience. The post is specially for research and teaching duties are limited. The holder will take part in high or low energy nuclear physics research, using either a 400 MeV. synchro-cyclotron or a 12 MeV. tandem Van der Graaff electrostatic generator. (b) Three posts of Assistant Lecturer or Lecturer. The initial salaries will be in the range £900 to £1,650 per annum for one post, and in the range £900 to £1,350 per annum for the other two. Each post carries normal teaching duties, and the holder will take part in research in one of the three following fields. (i) High energy physics using a 400 MeV. cyclotron. (ii) Low energy nuclear physics using a 12 MeV. tandem Van der Graaff electrostatic generator. (iii) Acoustics.

Applications, stating age, qualifications and experience, together with the names of three referees, should be received not later than March 1, by the Registrar, from whom further particulars of the conditions of employment may be obtained. Ref: CV/N.

UNIVERSITY OF ST. ANDREWS

Applications are invited for the post of Lecturer in Clinical Chemistry in the Department of Pathology, Queen's College, Dundee, and the Royal Infirmary, Dundee (549 beds), to undertake research and undergraduate teaching and to assist with the development and provision of a wide range of hospital services. New laboratories will be available later this year. Salary scale—medically qualified: £1,050 by £100 to £2,350 (efficiency bar £1,550); non-medically qualified: £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar £1,400). Appointment below efficiency bar in either case. F.S.S.U. Family allowance. Grant towards furniture removal. Candidates without medical qualification should preferably possess an honours degree in biochemistry or chemistry.

Applications (six copies), containing the names of three referees, to the undernoted, not later than March 4, 1961.

PATRICK CUMMING,
Joint Clerk to the University Court.
Queen's College, Dundee.

UNIVERSITY OF LONDON
KING'S COLLEGE

The College will require from Easter, 1961, if possible (failing that, on October 1), an Assistant Lecturer in Geology. Candidates should have a good Honours degree with special interests in mineralogy.

Salary scale: £800 by £50 per annum to £950, plus London allowance of £60, family allowances, and F.S.S.U. benefits.

Full conditions of appointment and application forms may be obtained from the Registrar, King's College London, Strand, W.C.2. Completed forms must reach him by February 28.

MORGAN CRUCIBLE

Research Laboratories want

TWO PHYSICAL CHEMISTS

● SENIOR TEAM LEADER (Ref 5)

A Ph.D. with several years experience of post-doctorate research in a university or high class industrial research laboratory. Only men with proven ability in leadership and the facility for producing and exploiting original ideas will be considered.

● RESEARCH CHEMIST (Ref 47)

A more recent graduate with Ph.D., 1st or 2nd class hons., keen on industrial research but not necessarily with extensive experience.

Both posts will be in a laboratory concerned mainly with solid state chemistry, surface chemistry and the techniques used in high temperature research.

Familiarity with thermodynamics, reaction kinetics or solid state diffusion would be an advantage, but is not essential.

This is an expanding research organization and these are responsible posts with excellent opportunities for advancement.

Please reply quoting reference to:

Manager, Staff Recruiting and Training,
Morgan Research Laboratories,
The Morgan Crucible Company Limited,
Battersea Church Road,
London, S.W.11.

UNIVERSITY OF ALBERTA
DEPARTMENT OF CHEMISTRY
TEACHING ASSISTANTSHIPS

$2,200 to $2,700 for eight months are open to qualified students proceeding to advanced degrees. Nine hours per week of laboratory instruction required. Active research programmes in analytical, inorganic, organic, physical and theoretical chemistry. Travel allowance.

Apply to: Professor Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

UNIVERSITY COLLEGE HOSPITAL
GOWER STREET, W.C.1

Applications are invited for the appointment of Biochemist (basic grade) from April 4, 1961.

Written applications, with names of two referees, to T. F. W. Mackeown, Administrator and Secretary by February 25, 1961.

DEPARTMENT OF PHYSICS
UNIVERSITY OF WESTERN ONTARIO
LONDON, CANADA

Applications are invited for the positions of Assistant Professor and for Lecturer. Applicants should possess the Ph.D. degree or equivalent. Duties will involve undergraduate and graduate teaching and research. Salary, dependent on experience, $7,000 minimum and $5,500 minimum per annum.

UNIVERSITY OF READING

Microbiology of Dairying. Applications are invited for a Lectureship in the Department of Microbiology from persons having experience in the microbiology of milk and milk products.

Further particulars may be obtained from the Registrar (Room 22, O.R.B.), the University, Reading, by whom applications must be received not later than March 14, 1961.

DCL

CHEMICAL ENGINEERS

The Distillers Company Limited invites applications for appointments as Chemical Engineers at the Hull, Yorkshire, factory of the Chemical Division, where a wide range of organic chemicals are manufactured in bulk by a variety of large-scale chemical processes. These posts offer excellent prospects for further progress, both within the Division and elsewhere in the Industrial Group of the Company.

The factory is modern and expanding; the manufacturing area at present covers some 100 acres, and there are about 2,000 employees. At all times chemical engineers work on or very close to the plant itself; their duties embrace the detailed development of entirely new projects, including process design, equipment design, costing and instrumentation, and modifications of existing plant and processes, with a view to increasing their efficiency.

Candidates for these posts, aged not over 30, must hold a good honours degree in Chemical Engineering, or an equivalent qualification; experience of chemical plant design or operation in the chemical or allied industries would be an advantage.

The Company operates a non-contributory pension scheme.

Write: STAFF MANAGER

THE DISTILLERS COMPANY LIMITED,

21 22 BOLTON STREET, LONDON, W.1.

Quote Ref.: 6/61 N.

HISTORICAL ARCHAEOLOGIST

required by

Department of Northern Affairs and National Resources, Ottawa

$6,840 to $7,860

To plan and conduct a programme of archaeological investigations concerned with the identification and restoration of Canadian Historical sites.

Candidates must be university graduates, preferably with an M.A. in Archaeology and possess a number of years of experience in conducting archaeological investigations, including the excavation of historical ruins.

For further details and application forms, please write to the Civil Service Commission of Canada, Ottawa, Ontario, and ask for Information Circular 61-470. Closing date for receipt of applications is March 31, 1961.

TECHNICIAN (FEMALE) AGE 25 to 32 years wanted. Duties flexible would include responsibility for sterilization of surgical equipment and other biological or chemical work. "A" level in chemistry and biology, S.R.N. or I.M.L.T. training or equivalent an advantage.—Apply in own handwriting, giving age, education and experience, to Administrator, University Laboratory of Physiology, Oxford.

BIOCHEMISTS OR CHEMISTS (TWO) REquired to assist in research on: (a) Column chromatography of proteins, (b) Blood lipids in relation to coagulation. Appointment for one year in the first instance. Possibility of work for higher degree.—Applications to Professor N. F. Maclagan, Department of Chemical Pathology, Westminster Medical School, London, S.W.1.

TECHNICAL ASSISTANT, MALE OR FEmale, aged 25 to 30, required in Intelligence Department of British Aluminium Company (London, S.W.1) to deal with technical inquiries and to abstract technical literature. Graduate preferred, knowledge of foreign languages desirable. Salary in accordance with age and previous experience.—Applications, in writing, stating full particulars, to Box N243 LPE, 60/62 St. Martin's Lane, London, W.C.2.

RESEARCH ASSISTANTSHIP OPEN September, 1961, on solid state physical chemistry of mucopolysaccharides. Research can be used for thesis for Ph.D. degree. Stipend $3,000 per year plus remittance of travel expense up to $200.—Candidates having Master degree or equivalent training apply to Dr. Bettelheim, Adelphi College, Garden City, New York, U.S.A.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND

To meet the needs of an increasing enrolment and an expanding programme, the Memorial University of Newfoundland invites applications for the following positions for 1961-1962, appointments to become effective September 1, 1961.

FACULTY OF ARTS AND SCIENCE

Department of Biology. An Assistant Professor, preferably with experience in Marine Biology, to teach and do research in Invertebrate Zoology. An Assistant Professor, with similar experience, to teach in Physiology, Embryology and Histology and develop programme of research in marine animal physiology.

Department of Chemistry. An Assistant Professor of Analytical or Physical Chemistry for teaching and research in his area of speciality.

Department of Mathematics. An Assistant or Associate Professor for undergraduate teaching.

Department of Physics. An Assistant Professor of Nuclear Physics (low energy) and an Assistant Professor of Theoretical or Atmospheric Physics to teach up to the Master's level and for research in his area of specialization.

The salary scale is: for Lecturer, up to $5,800; for Assistant Professors $6,500 to $7,000; for Associate Professors, $8,000 to $8,500.

The University will be moving to a new campus during the summer of 1961 and adequate facilities will be available for research. All appointments are provisional for two years. The University has a liberal contributory pension scheme. Travel expenses incurred in taking up an appointment are payable up to a maximum of $750.

Applications should be sent immediately, and preferably by airmail, to the President, Memorial University of Newfoundland, St. John's, Newfoundland, Canada, giving a complete curriculum vitae, the names and addresses of three referees and enclosing a recent photograph. Applicants should also lodge one copy of their application with the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1.

UNIVERSITY COLLEGE OF SWANSEA

LECTURESHIP OR ASSISTANT LECTURESHIP IN BOTANY

Applications are invited for the above post from candidates with a special interest in plant physiology or biophysics. The appointment will date from October 1, 1961. The person appointed will assist in the teaching of plant physiology and take particular responsibility for the supervision of practical classes in this subject. Salary scales: Lectureships, £1,050 to £1,850 per annum; Assistant Lectureships, £800 to £950 per annum. F.S.S.U. benefits and family allowances.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies) must be received not later than Saturday, March 11, 1961.

UNIVERSITY COLLEGE OF SWANSEA

TECHNICAL OFFICER IN THE DEPARTMENT OF BOTANY

Applications are invited for the post of Technical Officer to be responsible for the general supervision and maintenance of the laboratories and the control and training of technical staff in the Department of Botany. Applicants should have a University degree in science or equivalent qualification, and be interested in the application and development of techniques for teaching and research in Botany and/or Biochemistry. The appointment will be on the scale £700 by £50 to £1,050 (bar) by £50 to £1,300. Superannuation under F.S.S.U. and family allowances.

Applications (six copies) must reach the Registrar, from whom further particulars can be obtained, not later than Saturday, March 11, 1961.

McMASTER UNIVERSITY

GRADUATE ASSISTANTSHIPS IN CHEMISTRY

Applications are invited for Assistantships from persons qualified to pursue M.Sc. and Ph.D. work in Chemistry. Assistantships carry a yearly stipend of $2,200 to $2,800 and require eight to twelve hours per week of assisting from September to April only. The Department has excellent research facilities and provides opportunities for research in most branches of chemistry.

Further information concerning assistantships, scholarships and research in progress in the Department may be obtained from D. B. MacLean, Chairman, Department of Chemistry, McMaster University, Hamilton, Ontario, Canada.

UNIVERSITY OF ALBERTA
DEPARTMENT OF CHEMISTRY
POSTDOCTORAL FELLOWSHIPS

$5,500 tax free for 12 months, in all areas of chemistry.

Apply: H. E. Gunning, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

UNIVERSITY OF READING

Applications are invited for a post of Lecturer or Assistant Lecturer in Psychology.

Further particulars may be obtained from the Registrar (Room 22, O.R.B.), the University, Reading, by whom applications should be received not later than March 18, 1961.

UNIVERSITY OF READING

Microbiology. Applications are invited for a Lectureship in the Department of Microbiology, from persons having experience in food microbiology, preferably with some research experience. The post will be concerned with the institution of a new degree course in Food Science.

Further particulars may be obtained from the Registrar (Room 22, O.R.B.), the University, Reading, by whom applications must be received not later than March 14, 1961.

UNIVERSITY OF HULL

Applications are invited for appointment to an Assistant Lectureship in Physical Chemistry tenable from October 1, 1961. Salary £800 to £950 per annum with F.S.S.U. and family allowances.

Further particulars may be obtained from the undersigned to whom applications (six copies), should be sent not later than March 6, 1961.

W. D. CRAIG,
Registrar.

NATIONAL INSTITUTE OF AGRICULTURAL BOTANY
ASSISTANT SYSTEMATIC BOTANIST

Applications are invited for the post of Assistant Systematic Botanist. Applicants should be honours graduates in botany or agricultural botany. Starting salary at age 26 or over £965, maximum of scale £1,510. Superannuation under F.S.S.U.

Further particulars and application forms from M. G. Tozer, Secretary, N.I.A.B., Huntingdon Road, Cambridge.

CARLETON UNIVERSITY
OTTAWA, CANADA

Applications are invited for the position of Assistant Professor of Physics. Salary range is at present $6,500 to $8,500. The main research interest of the Department is in the field of dielectrics, and there are excellent facilities for this research. Ottawa is a centre of government research activity, and co-operation with other laboratories in the Ottawa area is encouraged. Many regular specialist seminars and symposia are held in the district.

Please apply to Dr. John Hart, Carleton University, Ottawa, Canada.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Research Technician required in Chester Beatty Research Institute, Fulham Road, S.W.3. Ordinary National Certificate or "A" level chemistry standard, with interest in organic chemistry, to do synthetic work in the heterocyclic amino acid fields. Superannuable; salary according to age, qualifications and experience on M.R.C. scales.—Applications, with names of referees, to the Secretary, 33 Sumner Place, S.W.7, quoting 301/B/49.

UNIVERSITY OF READING. APPLICATIONS are invited for an Assistant Lectureship or Lectureship in Microbiology from graduates in microbiology, bacteriology, botany, biochemistry or cognate fields. An interest in mycology and algae is desirable. The appointment will date from September 30, 1961.—Further particulars may be obtained from the Registrar (Room 22, O.R.B.), the University, Reading, by whom applications should be received not later than February 28, 1961.

NUCLEAR CHEMISTRY GRADUATE APpointments open beginning July or September, 1961, at stipends from $1,920 to $2,520 for fundamental work toward M.S. or Ph.D. degree. Twelve-month appointment with one month vacation. Excellent equipment for research on neutron induced nuclear reactions and decay schemes of radioactive nuclei using 400 KV. Cockcroft-Walton ion accelerator.—Write: Department of Chemistry, University of Arkansas, Fayetteville, Ark., U.S.A.

GUY'S HOSPITAL MEDICAL SCHOOL
LONDON BRIDGE, S.E.1

Applications are invited for a post of Lecturer or Senior Lecturer in the Bacteriology Department. Candidates should have a medical or scientific degree and an interest in a fundamental approach to microbiological problems. Salary within the following ranges: Lecturer (non-medical), £1,250 to £1,850 plus £60 London allowance or (medical), £1,350 to £2,200; Senior Lecturer (non-medical), £1,650 to £2,225 plus £80 London allowance or (medical), £2,000 to £2,400, according to qualifications and experience, with superannuation and family allowance.

Applications should be made on a form obtainable from the Dean not later than February 21, 1961.

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Young graduate, preferably with an honours degree, is required to join a team engaged on germanium and silicon devices. The sphere of activity embraces the development of processes necessary for products of high reliability in a variety of applications.

Preference will be given to applicants with previous experience of semiconductors who are within the age range 23 to 30.

Write in the first instance to Group Personnel Services, English Electric House, Strand, London, W.C.2, quoting reference N1506N.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Applications are invited for a Lectureship in Pure Geochemistry from October 1, 1961. Salary range £1,050 to £1,850 per annum plus £60 London allowance, F.S.S.U. membership and family allowances. Candidates should have geochemical qualifications and be familiar with one or more of the following techniques: optical or X-ray spectrography, silicate or radioactive analysis.

Apply to Professor D. Williams, Department of Geology, Imperial College of Science and Technology, London, S.W.7.

UNIVERSITY OF ALBERTA
DEPARTMENT OF CHEMISTRY
POSTDOCTORAL RESEARCH APPOINTMENTS

$6,000 per annum, tenable for a period of one to two years, in the areas of organic, physical organic, theoretical and physical chemistry.

Apply: H. E. Gunning, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

UNIVERSITY OF TORONTO
DEPARTMENT OF MATHEMATICS

Applications are invited for vacancies in the Applied Mathematics Section of the Department. Preference will be given to applicants with experience in quantum mechanics and fluid dynamics. Rank and salary will depend on qualifications and experience. Superannuation and removal allowances are available.

Applications should be sent to Professor D. B. DeLury, Chairman, Department of Mathematics, University of Toronto, Toronto 5, Canada.

PHYSICS LABORATORY TECHNICIAN (man or woman) required with experience of work in a teaching laboratory; prospects good; salary according to qualifications and experience on the scale of £490 to £675 plus London weighting.—Apply, Secretary, Royal Holloway College, Englefield Green, Surrey.

McMASTER UNIVERSITY
HAMILTON, ONTARIO

Applications are invited for Assistant and Associate Professor of Electrical Engineering. Candidates should be well qualified academically, preferably to the doctorate level, and should have some research, design or teaching experience in control systems. The duties include teaching at undergraduate and graduate levels, organization and direction of laboratory classes, conducting research and supervising research students. Salary scales are open and competitive with those of industrial and research establishments. Additional stipends are offered to professors who remain on the campus for eleven months of the year and carry out research during this period.

Applications should be addressed to the Chairman, Department of Electrical Engineering, from whom further information may be obtained.

ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY
GLASGOW
DEPARTMENT OF MATHEMATICS

Applications are invited for a Research Fellowship in Mathematics. The salary scale is £800 by £50 to £950, and the initial salary will depend upon qualifications. All appointments carry with them family allowances and membership of F.S.S.U.

Applications should be lodged with the Secretary of the College (from whom further details may be obtained) not later than March 16, 1961, and should include the names of two referees.

AMGUEDDFA GENEDLAETHOL CYMRU
(NATIONAL MUSEUM OF WALES)

Applications are invited for the post of Assistant Keeper in the Department of Botany. The appointment will be to either Grade 1 or Grade 2, according to age and experience. The successful applicant will be required to take up the appointment in November or December, 1961. The salary for Grade 2 is £775 to £1,092, and applicants must be under 30 years of age and possess an appropriate university degree. The salary for Grade 1 is £1,387 to £2,337, and applicants must possess an appropriate university degree and have museum experience. Contributory Superannuation (F.S.S.U.). Closing date for applications April 1, 1961.

Particulars and application forms from the Secretary, National Museum of Wales, Cardiff.

THE COTTON, SILK AND MAN-MADE FIBRES RESEARCH ASSOCIATION
(SHIRLEY INSTITUTE)

Abstractors are required for the Information Department. Applicants, who should be science graduates, and preferably, but not essentially, have knowledge of textile technology, must be capable of abstracting technical and scientific papers from foreign periodicals. The initial salary offered will depend upon qualifications and experience, and will carry superannuation under the Federated Superannuation System for Universities.

Applications, giving all relevant details, in handwriting, should be addressed to the Director, B.C.I.R.A., Shirley Institute, Didsbury, Manchester, 20.

LIBRARIAN FOR SCIENCE LIBRARY. Preferably with recognized library qualifications or appropriate university degree. Salary scale £625 (age 22), rising to £740 (25 or over), to £1,154 (maximum). Superannuation.—Apply, with full particulars, including names of two referees, to Secretary, Glasshouse Crops Research Institute, Worthing Road, Rustington, Littlehampton, Sussex, within three weeks.

FELLOWSHIPS UP TO $3,000 PER ANNUM available for qualified students proceeding to M.Sc. and Ph.D. degrees. Active research programmes in Biochemistry, Physical, Polymer, Organic, and Analytical Chemistry. Excellent research facilities in new laboratories.—Write Dr. H. H. G. Jellinek, Chemistry Department, Essex College, Assumption University, Windsor, Ontario, Canada.

RAMSAY MEMORIAL FELLOWSHIPS FOR Advanced Students of Chemistry. The Trustees will consider in June applications for a Fellowship, normally tenable for two years. Value £700 per annum, plus expenses grant of up to £100 per annum.—Further particulars from Joint Honorary Secretaries, Ramsay Memorial Fellowships Trust, University College London, Gower Street, W.C.1. Completed application forms must be received by April 17, 1961.

UNIVERSITY COLLEGE OF WALES
ABERYSTWYTH

Applications are invited for the post of Assistant Lecturer or Lecturer in the Department of Pure Mathematics to take up duties on October 1, 1961. Salary scales: Lecturer, £1,050 to £1,850; Assistant Lecturer, £800 to £950, plus Superannuation benefits and children's allowances.

Further particulars can be obtained from the Registrar, to whom applications should be sent, together with the names of two persons to whom reference may be made, not later than March 13, 1961.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Technician at the Marine Biological Station, Port Erin, Isle of Man. Basic salary in the range £490 to £675 per annum. Supplementary payments to basic salary will be made for possession of appropriate qualifications.

Applications, in writing, giving the names of two referees and quoting reference number 260/N, to the Registrar, the University, Liverpool 3.

COMMONWEALTH BUREAU OF HELMINTHOLOGY

Helminthologist required as Scientific Assistant to prepare abstracts and assist in editorial work on *Helminthological Abstracts*. Experience in helminthology and degree essential. Salary scale £738 to £1,872 with F.S.S.U. Starting salary according to age, qualifications and experience.

Apply to Acting Director, the White House, 103 St. Peter's Street, St. Albans, Herts, from whom further particulars may be obtained. Applications should be received by March 11, 1961.

UNIVERSITY OF NOTTINGHAM
DEPARTMENT OF AGRICULTURAL SCIENCES

Applications are invited for a Demonstratorship in Agricultural Botany and a Demonstratorship in Agricultural Zoology, at the School of Agriculture, Sutton Bonington. Salary scale: £550 by £25 to £600 per annum. Applications will be considered from candidates who expect to graduate this year.

Conditions of appointment and form of application to be returned as soon as possible, from the Registrar.

A GRADUATE WITH EXPERIENCE IN the field of anaerobic vaccines is required to supervise production and carry out development work on existing and new products. A young team is engaged in research and development and the post advertised is designed to augment the present effort with a bias towards production. The Institute is part of a large international organization with pharmaceutical interests and is situated in a rural area; transport from Cambridge is provided. The position will carry a generous salary, with pension and life assurance arrangements. A five-day week is worked with three weeks annual holiday.—Apply, giving details of experience, etc., to the Director, Bayer Biological Institute, Exning, near Newmarket, Suffolk.

METALLURGISTS AND PHYSICISTS REquired for crystallography and for studying high temperature materials and uranium alloys. Applicants should preferably have a good honours degree and postgraduate experience. Salaries for three vacancies in the range £1,000 to £1,500 per annum. Superannuation scheme. Applications to: Director of Research, Fulmer Research Institute Ltd., Stoke Poges, Buckinghamshire.

AGRICULTURAL RESEARCH COUNCIL. Ditton Laboratory requires a Plant Physiologist for investigation of effects of temperature, oxygen and carbon dioxide on the respiration of fruit. Good honours degree in botany and research experience essential. Starting salary in Senior Scientific Officer scale (£1,302 to £1,604) or £717 to £1,186 according to age and experience. F.S.S.U.—Applications, with names of three referees, to Director, Ditton Laboratory, Larkfield, Maidstone, Kent, within three weeks.

MISCELLANEOUS

THE PROPRIETORS OF BRITISH PATENT No. 698980 for "Ionizing Radiation Detector," are prepared to enter into negotiations for the sale or for the grant of licences thereunder.—Inquiries to be addressd to Carpmaels and Ransford, 24 Southampton Buildings, Chancery Lane, London, W.C.2.

THE PROPRIETORS OF BRITISH PATENT No. 732,004 for "Polarization Interferometer," are prepared to enter into negotiations for the sale or for the grant of licences thereunder.—Inquiries to be addressed to Carpmaels and Ransford, 24 Southampton Buildings, Chancery Lane, London, W.C.2.

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LECTURES AND COURSES

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The whole-time course for the University of London's Academic Postgraduate Diploma in Applied Parasitology and Entomology lasts for one academic year and is designed for candidates suitably qualified in medicine, veterinary medicine, veterinary science or science who wish to take up research or laboratory appointments abroad.

Applications for the course which begins next on September 25, 1961, must be received by April 1, 1961. The number of places is strictly limited. The fee is £73 10s.

UNIVERSITY OF LEEDS
ADVANCED COURSES IN X-RAY CRYSTALLOGRAPHY

Applications are invited from graduates in chemistry and physics for admission to this two-year course, starting in October, 1961. The D.S.I.R. has accepted the course as suitable for the tenure of its Advanced Course Studentships. Suitably qualified applicants will be given opportunities to work for higher degrees.

Applications and inquiries should be addressed to Dr. M. R. Truter, Department of Inorganic and Structural Chemistry, The University, Leeds, 2.

A ONE-DAY SYMPOSIUM on ADSORPTION AT LIQUID SURFACES

will be held on Friday, April 14, 1961 from 9.30 a.m. to 5 p.m.

Subjects included are the micellar state, monolayers of proteins and other polymers and adsorbed films of colloidal electrolytes.

Further details may be obtained from the Registrar, Bradford Institute of Technology, Bradford, 7.

UNIVERSITY OF EDINBURGH
POSTGRADUATE SCHOOL OF APPLIED DYNAMICS

A postgraduate course leading to the Diploma in Applied Dynamics of the University will be given in the Department of Engineering from October, 1961, to June, 1962. Lectures will be given on mechanical vibration, gyrodynamics and automatic control. Each student will also undertake a supervised research problem in one of these subjects. The D.S.I.R. has accepted the course as suitable for the tenure of its Advanced Course Studentships. Candidates who wish to be considered for these awards should apply to the University as soon as possible but not later than February 28, 1961.

Further particulars and application forms may be obtained from the Faculty of Science Office, Department of Chemistry, West Mains Road, Edinburgh, 9.

CHARLES H. STEWART,
Secretary to the University.

MIDDLESEX HOSPITAL MEDICAL SCHOOL
LONDON, W.1
DEPARTMENT OF PHYSICS AS APPLIED TO MEDICINE
FULL-TIME DAY COURSE IN RADIATION HAZARDS AND SAFETY

A course, extending over four weeks, will commence on Monday, October 16, 1961, and will provide an introduction to the subject suitable for medical, engineering, chemical and other professional workers whose duties require an overall appreciation of the problems involved in maintaining radiological safety in the utilization of radiations and radioactivity in industry and medicine.

The course will consist of lectures, demonstrations and practical work dealing with: Radiation Physics; Radiation Chemistry and Biology; Applications of Radiation in Industry and Medicine; Radiation Effects on Humans; Radiological Protection; Health Problems arising in the Nuclear Energy Industry.

Applications for admission to the course should be made to the Secretary, Department of Physics as Applied to Medicine, Middlesex Hospital Medical School, London, W.1, from whom further details of the course can also be obtained. The fee for the course will be £40.

KENT EDUCATION COMMITTEE
MEDWAY COLLEGE OF TECHNOLOGY
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Principal: H. R. Orr, B.Sc., Ph.D.
DEPARTMENT OF SCIENCE
Head of Department: C. E. Seaman, B.Sc., Ph.D., F.R.I.C.

AUTOMATIC AND SEMI-AUTOMATIC METHODS IN ANALYSIS AND CONTROL

A symposium for industrial analytical chemists interested in recent developments in this field will be held on Thursday, March 16, 1961. The symposium will consist of a morning session devoted to lectures and discussion, followed in the afternoon by an exhibition with demonstrations by the leading manufacturers of commercially available equipment.

The fee for the course is £1, inclusive of lunch and light refreshments. Further details and registration forms may be obtained from the course organizer, Dr. D. T. Burns, Department of Science, Medway College of Technology, Horsted, Maidstone Road, Chatham. Closing date for registration March 9, 1961.

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UNIVERSITY OF LEEDS

ADVANCED COURSE IN ULTRA HIGH PRESSURE CHEMISTRY

(with applications to Geochemistry)

Applications are invited from graduates in chemistry, physics and mineralogy for admission to this two year course, starting in October, 1961, under the direction of Dr. R. S. Bradley. The D.S.I.R. has accepted this course as suitable for the tenure of its Advanced Course Studentships. Suitably qualified applicants will be given opportunities to work for higher degrees.

Applications and inquiries should be addressed to Dr. R. S. Bradley, Department of Inorganic and Structural Chemistry, The University, Leeds, 2.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

A Postgraduate course of lectures on Fire Hazard of Buildings, arranged by Dr. J. H. Burgoyne, will be given in the Department of Chemical Engineering in the week commencing Monday, March 13, 1961.

Further particulars from the Registrar, Imperial College, London, S.W.7.

GRANTS & SCHOLARSHIPS

NUFFIELD FOUNDATION

BIOLOGICAL SCHOLARSHIPS AND BURSARIES

The Nuffield Foundation, as part of its programme for the advancement of biological studies, is prepared to offer for the academic year 1961-62 a limited number of scholarships and bursaries to enable persons who have graduated in physics, chemistry, or mathematics or engineering, but who have had no training in a biological subject, to receive such training in biology as will enable them in due course to undertake research and teaching in the United Kingdom in the biological sciences. The scholarships, which are senior awards, are intended for persons who have already undertaken some postgraduate research in their own subject. The bursaries are intended to enable those who have recently graduated to complete a course of training in biological subjects including, if considered necessary, a full honours degree course in biology. In the case of both scholars and bursars the Foundation will pay the cost of university and/or college fees in addition to a maintenance award. Graduates of universities in the United Kingdom, of either sex and preferably between the ages of 22 and 35, are eligible to apply.

Applications for awards in 1961 must be received before April 1, 1961, by the Director, the Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1, from whom full particulars and application forms can be obtained.

L. FARRER-BROWN, C.B.E.,
Director of the Nuffield Foundation.

UNIVERSITY OF SASKATCHEWAN

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING

Applications are invited from honours graduates in chemistry and graduates in chemical engineering for Graduate Scholarships, Teaching Assistantships and Research Assistantships, of value $1,800 to $2,700. These are tenable for research and advanced study leading to the M.A., M.Sc., and Ph.D. degrees in chemistry or chemical engineering. Postdoctorate Fellowships awarded by the National Research Council of Canada are tenable at the University of Saskatchewan.

Requests for additional information and application forms should be addressed to the Head, Department of Chemistry and Chemical Engineering University of Saskatchewan, Saskatoon, Sask., Canada.

NATO GRANTS

for participation in the CANADIAN THEORETICAL PHYSICS SEMINAR

Two grants of value $750 (£268) each are being offered by the North Atlantic Treaty Organization on a competitive basis to students of theoretical physics from NATO countries to attend the Second Quadrennial Theoretical Physics Seminar of the Canadian Association of Physicists to be held August 13 to September 9 at the University of Montreal. The seminar features lecture series by outstanding theoretical physicists as well as informal discussion on physics.

For further information and application forms write Dr. D. D. Betts, Department of Physics, University of Alberta, Edmonton, Canada. Deadline for applications is April 15.

ROYAL HOLLOWAY COLLEGE

(UNIVERSITY OF LONDON)

POSTGRADUATE STUDENTSHIPS 1961-62

The Council of Royal Holloway College will shortly award a certain number of Postgraduate Studentships in Arts and Science, open to men and women graduates of any University. Successful candidates, if eligible in other respects, will be recommended for State Studentships in Arts and Studentships of the Department of Scientific and Industrial Research. Particulars may be obtained from the Registrar.

Applications should be forwarded to the Principal, Royal Holloway College, Englefield Green, Surrey, as soon as possible, the closing dates for the receipt of applications from Arts and Science candidates being March 1, 1961, and July 1, 1961, respectively.

UNIVERSITY OF LEICESTER

DEPARTMENT OF CHEMISTRY

Applications are invited for: (a) A Research Fellowship (£800 to £900 per annum for three years) for work with Professor M. C. R. Symons on the study of "unstable intermediates" including spectrophotometric and electron spin resonance measurements on free radicals, carbonium ions etc. (b) A Research Scholarship (£350 to £400 per annum for three years) to work on similar projects, but with a particular bias towards a study of radicals trapped in crystalline solids.

Applications, with particulars of qualifications and experience and the names of two referees, to be sent to the Registrar as soon as possible.

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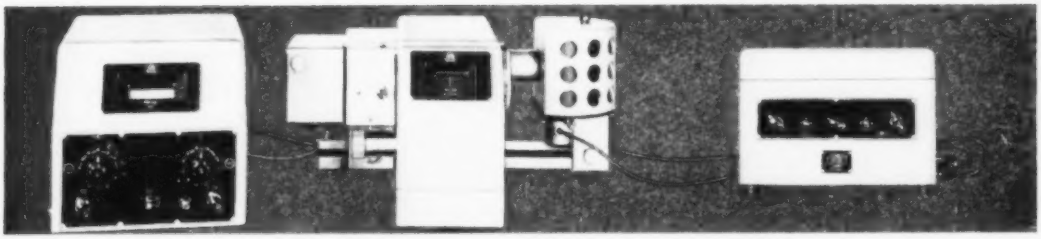

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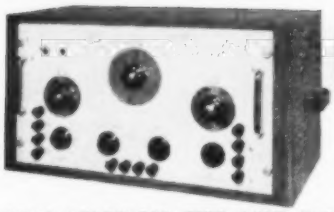

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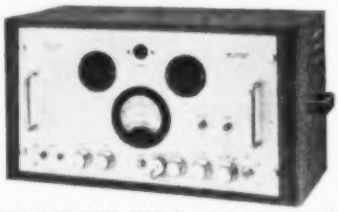

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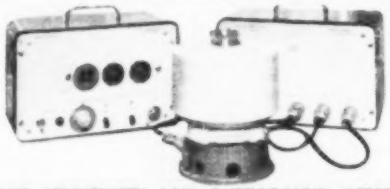

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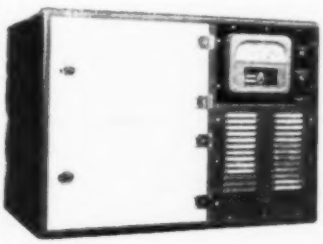

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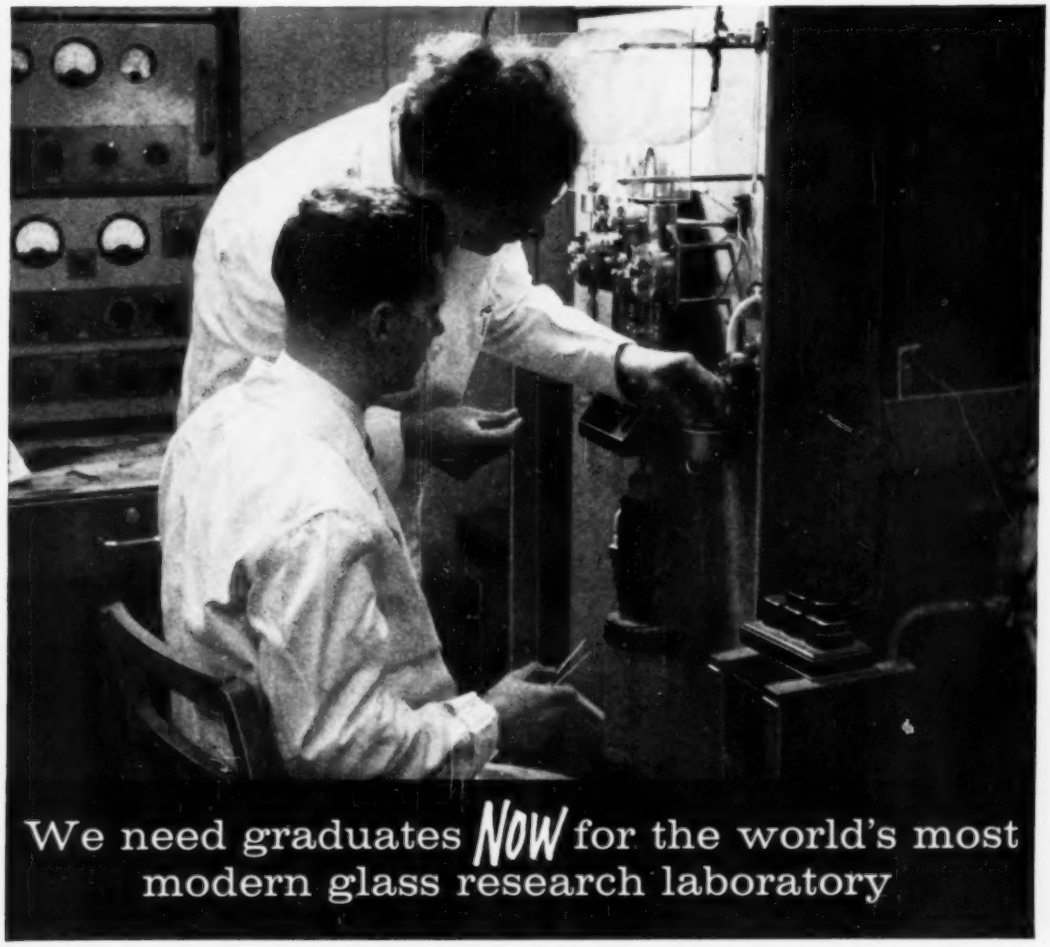

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available in densities from 2.5 to 6.2; of high quality and in best possible freedom from colour. Among these are several cerium stabilised types.

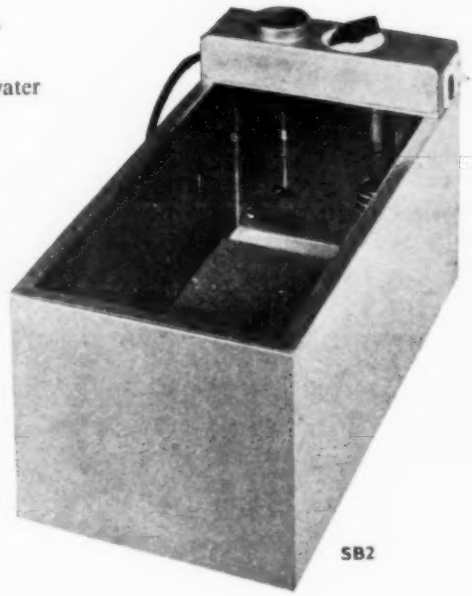
SCHOTT & GEN. MAINZ

JENA^ER GLASWERK SCHOTT & GEN., MAINZ

West-Germany

the standard laboratory bath

Stainless steel tank: Propeller stirring.
Dial marked in degrees Centigrade.
Available with pump for circulating water through other apparatus.
Wide range of test-tube racks, lids, cooling and constant level devices.
Unconditionally guaranteed for one year. Forty-eight hour repair service, and loan units available by return of post.



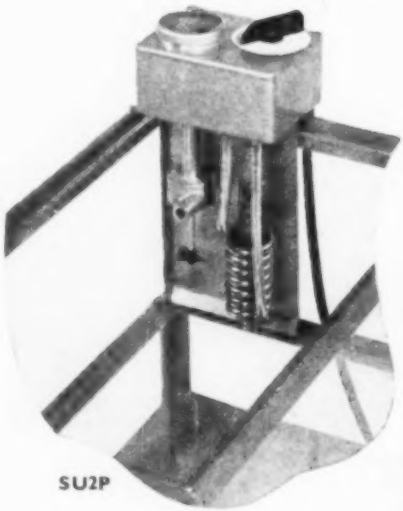
SB2

Standard Models
Range 10° to 100° C ±0·25° C

SB1 (9″×8″×6″) ...	£27 5 0
SB2 (15″×8″×6″) ...	£28 10 0
SB3 (21″×12″×11″)	£32 0 0
SB4 (15″×12″×9″)	£31 0 0

(working space in brackets)

thermostatic control unit



SU2P

MODELS SU2 and SU2P

This unit enables any vessel to be used as a thermostatically controlled bath. If fitted with a pump (as illustrated) it is particularly useful for circulating water at a controlled temperature through other apparatus. The heater, thermostat and stirrer are exactly as fitted to our standard baths.

Model SU2 (without pump) £19 10 0
Model SU2P (with pump) £22 10 0

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